THE PHILIPPINE
JOURNAL OF SCIENCE
B. TROPICAL MEDICINE

VOL. XII MARCH, 1917 No. 2

EXPERIMENTAL CHOLERA CARRIERS AND IMMUNITY[1]

By OTTO SCHÖBL and C. S. PANGANIBAN
(From the Biological Laboratory, Bureau of Science, Manila, and the Quarantine Laboratory, Health Officer's Department, Port of New York)

In order to gain some information with regard to the relation between immunity and the state of cholera carriers in experimental animals, it was necessary to establish first of all the presence or the absence of immune bodies in the blood of experimental cholera carriers, then the presence or the absence of immune bodies in the bile of immunized animals, and finally to study the influence of artificially produced immunity upon the existence and the duration of the state of cholera carriers in experimental animals.

It has been stated in one of the previous publications(1) that immunity has been found to exist as a result of intravesicular inoculation. This question was studied extensively with regard to various microbes by Viole.(2) This author found that the serum of rabbits infected by intravesicular injection of various microbes contained immune bodies in the blood and that the content of the infected gall bladder conveyed specific immunity to normal animals. The immunity as produced by intravesicular injection of bacteria is so closely related to the study of cholera carriers that it was deemed advisable to arrange some experiments in that direction.

[1] Received for publication December 13, 1916.

1. EXAMINATION OF THE SERUM OF EXPERIMENTAL CHOLERA CARRIERS FOR PRESENCE OF IMMUNE BODIES (AGGLUTININS)

Guinea pigs and rabbits were infected by intravesicular injection in the usual way.(3) The guinea pigs were bled from the carotid artery; the rabbits, from the ear vein. The same strain of cholera vibrio that was used to infect the animals was also employed in performing the agglutination test. The results of these tests are tabulated as follows:

TABLE I.—*Showing the presence of immune bodies in the serum of experimental cholera carriers (guinea pigs). Agglutination test.*

[++, strong agglutination; +, weak agglutination; + tr., trace of agglutination; —, no agglutination.]

CARRIER GUINEA PIGS.

Guinea pig.	Days after inoculation.	Dilutions of serum.					
		1/10	1/20	1/40	1/80	1/160	1/320
1	7	+ +	+ +	+	—	—	—
2	7	+ +	+ +	+	—	—	—
3	7	+ +	+ +	+	—	—	—
4	8	+ +	+ +	+ +	+	—	—
5	10	+ +	+ +	+ +	+	—	—
6	10	+ +	+ +	+ +	+	—	—
7	11	+ +	+ +	+ +	+	—	—
8	11	+ +	+ +	+ +	+	—	—
9	11	+ +	+ +	+ +	+	—	—
10	11	+ +	+ +	+ +	+	+ tr.	—
11	16	+ +	+ +	+ +	+	—	—
12	16	+ +	+ +	+ +	+	—	—

NORMAL GUINEA PIGS.

1		+ +	+ tr.	—	—	—	—
2		+ +	+ tr.	—	—	—	—
3		+ +	+ tr.	—	—	—	—
4		+ +	+ tr.	—	—	—	—
5		+ +	+ tr.	—	—	—	—
6		+ +	+ tr.	—	—	—	—

It is evident from Tables I and II that both guinea pigs and rabbits, the latter to a higher degree than the former, show the presence of immune bodies in the blood as a result of intravesicular inoculation with cholera vibrios.

TABLE II.—*Showing the presence of immune bodies in the serum of experimental cholera carriers (rabbits). Agglutination test.*

[++, strong agglutination; +, weak agglutination; + tr., trace of agglutination; —, no agglutination.]

CARRIER RABBITS.

Rabbit.	Days after inoculation.	Dilutions of serum.							
		1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280
1	0	+	—	—	—	—	—	—	—
	5	+ +	+ +	+ +	+ +	+	—	—	—
2	0	+	—	—	—	—	—	—	—
	6	+ +	+ +	+ +	+ +	+ +	+ +	+	—
3	0	+	—	—	—	—	—	—	—
	7	+ +	+ +	+ +	+ +	+	—	—	—
4	0	+	—	—	—	—	—	—	—
	10	+ +	+ +	+ +	+ +	+ +	+ +	+	—
5	0	+	—	—	—	—	—	—	—
	6	+ +	+ +	+ +	+ +	+ +	+	—	—
	12	+ +	+ +	+ +	+ +	+ +	+ +	—	—
	17	+ +	+ +	+ +	+ +	+ +	+ +	—	—
	22	+ +	+ +	+ +	+ +	+ +	+	—	—
	28	+ +	+ +	+ +	+ +	+ +	+	—	—
	38	+ +	+ +	+	—	—	—	—	—
	49	+ +	+ +	—	—	—	—	—	—
	57	+	—	—	—	—	—	—	—

The following experiment is included merely for the sake of completeness:

One rabbit was immunized by intravenous injections of $\frac{1}{10}$, $\frac{1}{5}$, $\frac{1}{2}$, and 1 slant of heated cholera culture. Twelve days after the last injection a sample of blood was withdrawn from the rabbit's ear vein and about 0.5 cubic centimeter of bile was aspirated from the animal's gall bladder by means of a syringe. Both the blood and the bile, which latter was of normal color and appearance, were subjected to agglutination tests in dilutions of from $\frac{1}{10}$ to $\frac{1}{1200}$. The serum of this rabbit agglutinated cholera vibrios promptly in all dilutions. No agglutination was noticed in the test tubes containing dilutions of the bile.

One rabbit was immunized by intravenous injections of $\frac{1}{10}$, $\frac{1}{5}$, $\frac{1}{2}$, and 1 slant of heated cholera culture. On the twelfth day after the last injection this animal was infected with $\frac{1}{10}$ of a slant of live cholera culture by intravesicular injection. Twenty-four hours after the infection the bile was withdrawn from the

gall bladder by means of a syringe. A sample of blood was also taken from the ear vein. The bile was of a light yellowish color and contained a large amount of mucus. No blood was found upon microscopical examination of the contents of the gall bladder. Centrifuged, it became clear and was subjected to the agglutination test. The serum showed positive agglutination in all dilutions up to $\frac{1}{1200}$. The contents of the gall bladder gave positive agglutination in dilutions $\frac{1}{10}$ and $\frac{1}{20}$. Since the results of this experiment as well as those of the preceding tests are in accord with the results arrived at by Viole in his studies on this particular question, it was thought unnecessary to extend our experiments any further. The most important facts bearing on the question of experimental cholera carriers, namely, the presence of immune bodies in the blood of experimental cholera carriers and their occurrence in the content of infected gall bladder in immunized animals, has been demonstrated. Considering the findings of Viole and our own, one is inclined to expect that vaccination should exert some influence upon the state of cholera carriers in experimental animals.

In order to decide this important question, the following experiments were arranged:

II. PREVENTIVE VACCINATION AND EXPERIMENTAL CHOLERA CARRIERS

A series of guinea pigs was immunized by injecting a suspension of cholera vibrios in physiological salt solution heated at 60° C. for thirty minutes. These injections were given either under the skin or intraperitoneally. At intervals of time, given in Table III, the vaccinated animals were infected with live cholera culture by intravesicular injection. One tenth of a slant of live cholera culture was injected. A series of normal animals, that is to say guinea pigs that had received no preventive treatment, was infected simultaneously and in the same manner as the immunized ones. At intervals varying from one to thirteen days after the intravesicular infection the animals were killed and the various sections of the digestive system were examined for the presence of cholera vibrios. The thirteenth day was taken as the upper limit of time, since it became known in previous experiments(3) that after the fourteenth day some of the experimental carriers became spontaneously negative.

TABLE III.—*Showing the number of takes and the duration of the state of cholera carriers in immunized and nonimmunized animals.*

[+, cholera vibrios found; —, cholera vibrios not found; vn, very numerous, more than 200 colonies; n, numerous, about 200 colonies; f, few, about 12 colonies; vf, very few, less than 6 colonies.]

Guinea pig.	Immunized.		Infected, days after vaccine.	Killed, days after infection.	Direct plates.				Peptone cultures.			
	Dose in slants.	Mode of immunization.			Bile.	Duodenum.	Ileum.	Cæcum.	Gall bladder.	Duodenum.	Ileum.	Cæcum.
1	1/10, 1/5, 1/2	Subcutaneous.	8	1	o	o	o	o	+	+	+	+
2	1/10, 1/5, 1/2, 1	do	8	5	n	f	f	—	+	+	+	+
3	1/10, 1/5, 1/2, 1	do	8	5	f	—	—	—	+	—	+	—
4	1/100, 1/20, 1/2, 1	Intraperitoneally.	8	5	n	n	f	—	+	+	+	+
5	1/10	Subcutaneous.	19	6	f	vf	f	—	+	+	+	+
6	1/10, 1/5	do	19	6	n	f	n	—	+	+	+	+
7	1/10, 1/5, 1/2	do	19	6	n	f	—	—	+	+	+	+
8	1/100	Intraperitoneally.	10	7	n	f	f	—	+	+	+	+
9	1/100, 1/50	do	10	7	n	n	n	—	+	+	+	+
10	1/100, 1/50, 1/20	do	10	7	n	n	n	f	+	+	+	+
11	1/10, 1/5, 1/2, 1	Subcutaneous.	10	9	vf	—	vf	—	+	—	+	—
12	1/10, 1/5, 1/2, 1	do	10	10	vf	—	vf	—	+	—	+	—
13	1/10, 1/5, 1/2, 1	do	10	13	—	—	—	—	—	—	—	—
14	1/10, 1/5, 1/2, 1	do	10	14	vn	—	n	—	+	+	+	+
15	1/10, 1/5, 1/2, 1	do	10	14	—	—	—	—	+	—	—	—
16	1/10, 1/5, 1/2, 1	do	10	14	f	vf	—	—	+	+	+	—
NONIMMUNIZED CONTROLS.												
17				5	f	—	f	vf	+	+	+	+
18				5	n	n	n	vf	+	+	+	+
19				7	n	f	f	vf	+	+	+	+
20				9	vf	—	vf	—	+	—	+	—
21				10	vf	—	vf	—	+	+	+	+
22				13	vf	—	vf	—	+	+	+	—
23				14	n	vf	—	—	+	+	+	—
24				14	n	—	—	—	+	+	+	—
25				14	—	—	—	—	+	—	—	—

III. VACCINE THERAPY OF EXPERIMENTAL CHOLERA CARRIERS

A series of guinea pigs was infected by intravesicular injection. After the infection some of these animals were vaccinated by subcutaneous injection of heated cholera cultures. From seven to thirteen days after the infection they were killed and examined. The thirteenth day was taken as the upper limit for the reason already given.

TABLE IV.—*Showing the duration of the state of cholera carriers in treated and in untreated animals.*

[+, cholera vibrios found; —, cholera vibrios not found; vn, very numerous, more than 200 colonies; n, numerous, about 200 colonies; f, few, about 12 colonies; vf, very few, less than 6 colonies.]

Guinea pig.	Treatment.		Mode of immunization.	Killed after infection.	Days after last vaccine.	Direct plates.				Peptone cultures.			
	Days after infection.	Dose of vaccine in slants.				Bile.	Duodenum.	Ileum.	Cæcum.	Gall bladder.	Duodenum.	Ileum.	Cæcum.
1	1	1/10	Subcutaneous.	7	6	vn	—	f	—	+	+	+	—
2	1	1/10	do	3	2	vn	n	vn	f	+	+	+	+
3	6	1/10	do	7	1	vn	vn	vn	—	+	+	+	—
4	1	1/10, 1/5, 1/2	do	9	6	f	vf	—	—	+	+	+	+
5	1	1/10, 1/5, 1/2	do	9	3	n	n	n	f	+	+	+	+
6	4	1/10, 1/5	do	10	4	vf	—	—	—	+	—	+	—
7	4	1/10, 1/5	do	11	4	n	—	vf	—	+	—	+	—
8	4	1/10, 1/5	do	11	4	f	—	vf	—	+	+	+	+
9	1	1/10, 1/5	do	12		vn	vn	—	—	+	+	+	—
UNTREATED ANIMALS.													
10				9		n	vf	f	—	+	+	+	+
11				10		vn	n	f	—	+	+	+	—
12				11		n	—	vf	—	+	+	+	—
13				11		vn	f	n	f	+	+	+	+
14				12		vn	n	n	—	+	+	+	—

These tables show the results of experiments concerning the influence of immunization upon the state of experimental cholera carriers. Unless we interpret as an effect of immunization the one negative animal (guinea pig 13, Table III) and the apparent decrease of cholera vibrios in the intestinal canal, as indicated by absence of cholera colonies on direct plates, we fail to see any effect of immunization upon the cholera carrier state in experimental animals.

It must be admitted that the test is rather severe, because the mode of infection, namely, the introduction of a considerable amount of cholera culture directly into the gall bladder, gives the vibrios the best possible chance to gain a foothold in the gall passages. Again the short time of observation, limited to thirteen days after infection, hardly allows the immunity to develop the maximum of its action.

CONCLUSIONS

1. Specific immune bodies were found to be present in the blood serum of experimental cholera carriers (guinea pigs, rabbits).

2. Specific immune bodies were found to be absent in the normal bile of a highly immunized rabbit. In confirmation of Viole's findings specific antibodies were found to be present in the gall bladder contents of infected rabbits.

3. The percentage of takes in guinea pigs that received preventive inoculation or vaccine treatment was as high as in untreated carriers.

4. Preventive vaccination and vaccine therapy effected no apparent shortening of the duration of cholera carriers in guinea pigs.

REFERENCES

(1) *Journ. Inf. Dis.* (1916), **19**, 145.
(2) *Ann. Inst. Pasteur* (1912), **26**, 147, 381.
(3) *Journ. Inf. Dis.* (1916), **18**, 307–314.

STUDY OF THE ANATOMICOPATHOLOGIC LESIONS IN ONE THOUSAND FILIPINO CHILDREN UNDER FIVE YEARS OF AGE [1]

By MARIA PAZ MENDOZA-GUAZON

(From the Department of Pathology and Bacteriology, College of Medicine and Surgery, University of the Philippines)

The purpose of this work is to tabulate the anatomicopathologic lesions of Filipino children under 5 years as found at autopsy, for the purpose of comparison with the published results of workers in other countries and to find the influence of age and season on certain diseases. The majority of the cases came from the Philippine General Hospital, some from San Lazaro Hospital for communicable diseases, and a few from other sources.

This record does not indicate the causes of infant mortality in the city of Manila, yet it reflects them to a certain degree.

The autopsies have been performed by the different members of the pathological staff of the College of Medicine and Surgery, University of the Philippines, and comprise those performed from January, 1910, to March, 1916, a total of 1,000 cases, in a period of a little over five years.

STILLBIRTHS

Of 52 cases of stillbirth, 5 gave unsatisfactory results from the standpoint of causation, owing in part to the unsatisfactory examination and in part to the insufficient knowledge of the maternal condition. Fifteen were premature and 5 were macerated fœtuses. Of the remaining 32, in which anatomical investigation showed definite lesions which could account for the stillbirth, the causes can be classified as follows:

Asphyxia in utero, 4 cases; knot in the cord, 1; fracture of the skull, 4; multiple congenital anomalies, 2; cerebral hemorrhage, 2; intraperitoneal cyst with calcareous deposits and chronic adhesive peritonitis, 1; cephalohematoma, 10; rupture of the anterior intervertebral ligament, 3; hemorrhage into the adrenals (forceps case), subdural hemorrhage and atelectasis of the lungs and hyperplasia of the thymus gland, which weighed 87

[1] Thesis presented for the degree of Doctor of Tropical Medicine, 1916. Received for publication February, 1917.

grams, craniotomy, cleidotomy, ectopic gestation with peritoneal implantation of the placenta, and gelatinous mass in the abdomen (probably meconium), 1 each. Eight of the cases of cephalohematoma had meningeal hemorrhage, 2 subcapsular hemorrhage of the liver, and 1 hemorrhage in the adrenals and kidneys.

CAUSES OF DEATH FROM THE FIRST TO THE SIXTH DAY

Causes of death, first day, 19 cases. Hemorrhage, 12 cases; congenital atelectasis of the lungs, 4; volvulus of the intestine, artificial anus with bronchopneumonia, acute enteritis with hepatic cirrhosis, 1 each. Of the 12 cases of hemorrhage, 10 were in the cerebrum or meninges, 1 of these being caused by rupture of hernia cerebri frontalis, 2 were in the adrenals, 1 was in the duodenum. The last case was in a premature male of 7 months, who also had a hematoma in the inferior border of the left lobe of the liver; rupture of the liver; hemorrhage into the peritoneum, the thorax, and the adrenals; and slight atelectasis of the lungs.

Second day, 5 cases. Hemophilia neonatorum, multiple congenital anomalies, imperforate rectum, congenital umbilical hernia with the liver and part of the intestines inside an umbilical sac, and comminuted fracture of the temporal bones, 1 each. The last had also hemorrhage into the peritoneum, liver capsule, and adrenals probably following resuscitation.

Third day, 11 cases. Six of these were due to the following causes: Hemophilia neonatorum, atresia recti with pulmonary hemorrhage and scoliosis, icterus neonatorum with pulmonary atelectasis in a premature infant, internal hydrocephalus in a male twin, and secondary anæmia caused by hemorrhage from the umbilical cord, which was cut very short. Of the remaining 5, 3 had hemorrhage into the lungs and brain. Besides the hemorrhage into the lungs and brain, patent ductus arteriosus was found in 2 cases of the former and patent foramen ovale in 1 case of the former and in 1 of the latter.

Fourth day, 2 cases. One had hemorrhage into the right cerebellar hemisphere and the other hemorrhage into the lungs, internal hydrocephalus, and patent ductus arteriosus and foramen ovale. The last was a premature male, 7 months old.

Fifth day, 8 cases. Hemorrhage, 5 cases; suppurative meningitis, action of rats, and congenital syphilis, 1 each. Of the 5 cases of hemorrhage, 4 were subdural and accompanied by icterus, 1 of these had omphalitis, another streptococcæmia-

following an infected cephalohematoma, and another acute membraneous enteritis, acute suppurative pancreatitis, acute choledochitis, and acute hemorrhagic nephritis. The case of suppurative meningitis had erosion of the skin covering a congenital sacral spina bifida (sacral meningomyelocele).(6)

Sixth day, 1 case. Hemorrhage in the lungs and acute gastroduodenitis.

From this we can see that hemorrhage played a great part in causing death during the first days of life, but we cannot take this as the rule in the city of Manila, for many of our cases came from the obstetrical department of the Philippine General Hospital, whose mothers asked help only when all the outside resources were exhausted.

Knopfelmacher(29) says that hemorrhage in the newborn occurs frequently in unassisted as well as in assisted labors. The hemorrhage is in part traumatic in origin, in part, however, due to interruption in the placental circulation through compression of the cord or through asphyxia.

Holt(27) thinks that the predisposing cause of the frequence of hemorrhage in young infants is due to the extreme delicacy of the blood vessels and the great changes taking place in the blood itself and in the circulation as a result of the passage from intrauterine to extrauterine life. Without taking into consideration those cases due to trauma and those due to infection, he mentions a class in which the hemorrhages are not associated with any other known process and in which the bleeding is extensive, multiple in location, and spontaneous in origin, and ceases also in the same way.

Cautley(8) divides the hemorrhagic diseases of the newborn into three: accidental, traumatic, and pyogenic. He states that in true hemorrhagic disease there is a spontaneous capillary oozing, which begins at a variable period after birth and proves fatal or lasts for a few days to a few weeks and yet ends in recovery. The circulatory disturbances due to ligature of the cord at birth or compression of the cord during labor may cause hyperæmia of the mucous membranes and hemorrhagic oozing and extravasation throughout the body. Similar congestion can be produced by backward pressure from congenital heart lesions, the respiratory obstruction in asphyxia and atelectasis, and hepatic cirrhosis. Gastrointestinal hemorrhage may thus be a kind of epistaxis from the congested membrane in consequence of its sudden functional activity, possibly associated with deficient coagulability of the blood.

Schloss and Commiskey,(46) after investigating the coagulation of the blood in 10 cases of the so-called hemorrhagic disease of the newborn, came to the following conclusions:

1. In the hemorrhagic conditions of the newborn the coagulation of the blood may be normal, delayed, or absent.
2. A deficiency or absence of thrombin or fibrinogen may give rise to imperfect blood coagulation and uncontrollable hemorrhage.
3. In some cases of hemorrhage in the newborn in which blood coagulation is apparently normal, it seems probable that the hemorrhage is due to some localized vascular lesion or defect present only in the areas from which the bleeding occurs.
4. The subcutaneous injection of whole blood is harmless and is of apparent value in the treatment of hemorrhage.

Shaw and Williams(47) found the coagulation time in infants under 2 years shorter than in adults.

Tabulating our cases of hemorrhage as to place found in this series of 1,000 autopsies of children under 5 years, we have:

Hemophilia neonatorum, 2 cases.

Hemorrhage in the lungs, 9 cases. In one of these the hemorrhage of the lungs was associated with hemorrhage in the meninges and liver, one with atresia ani, one with acute gastroduodenitis, and another had also intradural and basal hemorrhages of the brain.

Hemorrhage from the navel, 4 cases. Besides the hemorrhage, suppurative thrombophlebitis and bronchopneumonia were found in a 17-day-old infant.

Cerebellar hemorrhage, 6 cases. It is interesting to note the case of a premature infant that lived for fifty-one days with an old hemorrhage in the cerebellum and tuberculous mesenteric glands and that died of bronchopneumonia.

Subdural hemorrhage, 7 cases. In 5, atelectasis of the lungs was found; in 1, bronchopneumonia, icterus, and cirrhosis of the liver, and in the last, meningeal hemorrhage and omphalitis.

Brain and meningeal hemorrhages, 9 cases. One of these had also umbilical hemorrhage. In a baby 1 month old the hemorrhage became colliquative, and in another 8 months old it was located in the left parietal region and was organized.

Meningeal hemorrhage, 16 cases. Atelectasis of the lungs was found in 9, and cephalohematoma was found in 4; both conditions were met in 3 cases. The hemorrhage was so extensive in a female 3 months old that the clinicians diagnosed it as eclampsia.

Fracture of the skull and hemorrhage, 9 cases. One of these had also hemorrhage in the liver.

Retroretinal hemorrhage due to glioma, 2 cases.

Hemorrhage from the alimentary tract, 4 cases. One was from a gastric ulcer in a male 25 days old that died of lobar and lobular pneumonia and acute nephritis; 1 a duodenal ulcer and complicated with suppurative otitis media; 1 from the urinary bladder and accompanied by ulcerative enterocolitis; and the last had also hemorrhage in the duodenum, hematoma in the left lobe of the liver, and cerebromeningeal hemorrhage. Hemorrhage in the adrenals is a frequent occurrence either alone or with hemorrhage of the other organs. Of the first we had 3 cases, and of the latter we had 4.

Hemorrhage in the liver, 8 cases. Of these, 4 were accompanied by hemorrhage of the brain or meninges; 2 of the adrenals; and of 2, of both organs.

Rupture of the anterior intervertebral ligament at the level of the last cervical vertebra, 3 cases. This is probably due to extreme anteflection of the head in performing Moriceau's maneuver for extraction of the head.

ANOMALIES AND CONGENITAL DEFECTS

Heart and blood vessels, 21 cases.

Patent foramen ovale, 19 cases; patent ductus arteriosus, 36; patent interventricular septum, 4; displaced heart to the right side, 1; and presence of two cusps in the pulmonary orifice, 1. The small number of cases with patent foramen ovale and ductus arteriosus is probably due to incomplete examination on the part of the pathologist.

Brain. There has been one case of each of the following: Porencephalus, hernia cerebri, meningocele, sacral spina bifida, long cerebellar peduncles, and microencephalia. The pseudotetanic symptoms of the last have been reported by José Albert and M. P. Mendoza to the Philippine Medical Association (1912).

Genitourinary system, 16 cases. Horseshoe kidney, 2 cases; congenital cystic kidneys, 2; undescended testicles, 4; congenital hydrocele, 2; stricture of ureter, 1; left ureter coming from the lower anterior portion of the kidney, 1; cystic ovaries, 2; hernia of right tube and ovary in right inguinal canal, 1; bicornuate uterus, 1. One of the cases of undescended testicle had hernia in the right inguinal canal, and one of the cases of cystic ovaries was accompanied by patent interventricular septum. The infantile uterus has been found many times on the left side in my autopsies.

Alimentary tract. Tracheo-œsophageal anastomosis and multiple congenital anomalies, 1 case; imperforate rectum, 1; imperforate anus, 3; microcolon and omental adhesions, 1; gelatinous mass in abdomen, probably meconium, 1; congenital obliteration of the cystic duct with hydrops of the gall bladder, 1; congenital obliteration of the gall bladder, 1; cysts on either side of the œsophagus, 1; aberrant liver tissue in pancreas, 1; Meckel's diverticulum, 2; inguinal hernia, 2; congenital volvulus of the intestine 30 centimeters above the ileocæcal valve, 1. The last lived for one hour only, and at autopsy there was rupture of the ileum 2 centimeters below the twist. The 2 cases of hernia were found in males and in the right side.

Liver. Autopsy 3197 is a female infant that lived 39 hours. The liver and several loops of the small and large intestines were found inside a hernia of the umbilical cord. The small liver is entirely within the sac, except a small strip from the posterolateral edge of the left lobe that extends outward and downward to the anterior surface of the cardiac end of the stomach. The lower part of the Spighelian lobe is relatively enlarged and is directly in relation to the posterior surface of the lesser omentum.

Lungs. Left lung with three lobes, 2 cases; incomplete lobulation of the lungs, 1; malformation and misplaced right lung, which was found as a small mass beneath the left, 1; right lung with two lobes, 2.

Bones. Anomaly of fourth costal cartilage, 1 case.

Spleen. Accessory, 5 cases only are recorded.

Ectopic gestation with peritoneal implantation of the placenta, 1 case.

MULTIPLE CONGENITAL ANOMALIES

Autopsy 2111.—The mouth is very narrow, almost circular, and the buccal cavity just admits a leadpencil; the fourth and fifth fingers on each hand are fused; the inferior mandible is very pointed; the fourth and fifth toes are fused, and there is no uvula. Larynx is imperfectly developed, with cleft epiglottis and no vocal cords. Left kidney is cystic, right kidney and ureter missing. Lobes of liver symmetrical, and its median line is that of the abdomen. External genitalia are imperfectly developed, there being a small perforate organ which may represent penis or clitoris.

Autopsy 1932.—Male infant, born by breech presentation, with placenta attached by a short fibrous cephalic cord 1 centimeter in length, containing blood vessels which on dissection are con-

tinuous with the umbilical cord to a frontal meningocele. The fibers of the cephalic cord are continuous with the fœtal membranes and with the covering skin of the meningocele.

The head is incomplete; there is no forehead above the superciliary ridges, but immediately above the left inner canthus and left inner side of the nose is a semiglobular mass about 2 centimeters in diameter, yellowish and dry, which during life contained cerebrospinal fluid and brain substance. From the forehead extends upward and around the head just about the level of the tops of the ears a large, thin cystic mass. The hair below this is well developed. The nose and mouth are much deformed. The right ala nasi is apparently formed, but is separated from the median portion of the nose by the nostril, which extends halfway to the bridge. There is an opening on the left side where the ala nasi is apparently deficient, orifices leading both into the left nostril and into a cavity between the left inner canthus and nose. The upper lip shows two divisions like the ordinary cleft palate in the superior portion, which makes the mouth large and the hard palate much deformed.

The three outer fingers on the right hand are imperfectly developed and form a single mass with 3 fingernails; the three fingers cannot be differentiated. This mass is about half as long as the first finger. The first finger and thumb are well proportioned. On the left hand the same description applies to the outer two fingers.

On the left foot the first and second toes are missing, apparently no phalanges having developed; the other three are very short and rudimentary. The toes on the right foot are normally developed.

The eyes are perfectly developed, but the right has a smaller opening at the expense of the palpebral skin, so that it could not be voluntarily opened during life. The chest is well shaped, rounded, and wide, and is very large. This baby lived for nineteen days.

Autopsy 2146.—Male with malformation of hands, wrists, and left forearm, imperfect interventricular septum, and undescended right testicle. Only one bone could be palpated in the left forearm, and the carpal bones as individual bones appear to be absent. The left thumb was an outgrowth at the end of the first phalanx of the first finger on its inner and outer aspect and was loosely attached.

Autopsy 2282.—Male that lived for two days with the clinical diagnosis of absence of penis and imperforate anus. This case is

interesting, for the anomalies were found at the junction of the ectoderm and endoderm. The post-mortem description is as follows:

In the pubic area is a sac covered with skin resembling a scrotum. In the midlateral portion of this on the right side is a slitlike fold of the skin with the convexity upward, from which there exudes pale, turbid fluid on pressure of the sac. The cæcum is beneath the margin of the liver, and the appendix is lying on the anterior surface of it.

The œsophagus is of normal caliber and is lined by a pale mucosa, but it ends in a blind pouch at its mid portion. The cardiac end seems to be of normal caliber and appearance and passes directly into the lower end of the trachea between the primary bronchi. The mucosa of the bronchi is continued on to that of the trachea, on its anterior wall especially showing the longitudinal striations of the mucosa.

The stomach is small and empty. The opening of the œsophagus into the stomach is normal, but the pyloric end of the stomach forms a blind pouch, which does not communicate with the duodenum.

The right lung has only two lobes.

The ductus arteriosus is widely open, forming a canal about 0.5 centimeter in diameter. The foramen ovale is also patent.

The kidneys are fused into one, forming a horseshoe, the junction between them being placed at the lower poles and overlying the lumbar vertebra. There are two ureters.

The lower part of the abdomen is occupied by a large, hollow mass, which extends into the pelvis. This is attached to the urachus, and passing over it from the right to the left is a thick, but partially patent, hypogastric vessel. This sac has a thick wall, about 0.5 centimeter in thickness, and is lined by mucosa which is hemorrhagic in its upper portion and looks similar to that of the urinary bladder. Entering this sac are the ureters, which are laterally placed, and posteriorly and internally to the entrance of the right ureter at a point about the right margin of the promontory of the sacrum there enters the lower end of the dilated large intestine; this is very much constricted at its opening into this sac. From the lower portion of the sac, passing beneath the symphysis pubis, is a narrow canal which almost immediately bulges out to form a large sac, this sac being in the interior of the sac which was described as occupying the scrotal region. It is lined by smooth pale mucosa and a small circular orifice which just admits a small probe communicating with the slitlike opening, which was described on the right

lateral margin of the scrotal sac. The large sac and that which is called the scrotal sac are filled with brownish yellow globular masses of a rather firm consistence with some turbid fluid, both being present also in the dilated large intestine.

Finkelstone and Ellis(17) reported the case of a full-term child with œsophagotracheal fistula. The œsophagus ended in a blind pouch at the fifth tracheal ring from the bifurcation, and at the third tracheal ring from the bifurcation the distal end of the œsophagus opened into the trachea, causing a stricture at this site. Macroscopically they did not find any continuity of the œsophagus between the third and fifth ring, not even a fibrous cord. The stricture, they think, is due to an overgrowth of cells, either endodermal or ectodermal or a combination of the two at the junction of the œsophagotracheal fistula.

They cite two important theories about this, that of St. Clair Thomson and that of Locee. The first says that it is an arrest of development rather than a pathological process in the fœtus, while the second explains it embryologically, that is, that the proximal and distal portions of the œsophagus have different sources of origin. The buccal cavity, pharynx, and upper extremity of the œsophagus develop from the ectoderm, and the intestinal tract, including the distal portion of the œsophagus and respiratory apparatus, develop from the entoderm. Fistulous communications between œsophagus and trachea are almost always situated at its bifurcation, and the membrane separating them closes last at this location.

Autopsy 1577.—In this case the urethra opens near the exterior into a common passage with the rectum.

Autopsy 4062.—This male premature infant lived for about fifteen minutes after delivery. The clinical diagnosis of this case is hydramnios, and at autopsy there was found in the right side of the abdomen partly extending into the left side and into the pelvis and to the liver a greenish, very soft gelatinous mass of about 500 grams in weight. Intermingled throughout this there are small spherical bodies of 0.5 centimeter in diameter; these have a pale capsule surrounding them and contain a greenish gelatinous material. Some of these whitish bodies are located beneath the peritoneum over the anterior surface of the left kidney, and over the entire abdominal viscera there is a thin, delicate structure. The liver and spleen are adherent to the diaphragm. Over the coils of the small intestine in the right half of the abdomen is a greenish membranous structure binding them together. A similar case was autopsied after this series.

Dr. B. C. Crowell, pathologist, College of Medicine and Surgery, University of the Philippines, thought that the cause was an antenatal rupture of the intestine with peritonitis.

Autopsy 4170.—This female full-term baby lived for one month and fifteen days and died with an undetermined diagnosis. The anatomical finding is interesting, for the development of the heart and vessels and the cloacal region seem to have been arrested at the fifth month of fœtal life.

The anus is reddened and very small and measures about 0.5 centimeter in diameter. This has been operated for atresia ani. The labia majora are not distinct. There is a protrusion in the genital region about the clitoris which seems to be a fold inclosing two small leaflets that are apparently the labia minora. Between these is an opening for both the urethra and vagina. Fœcal material comes both from the artificial anus and genital opening. The relation of the urinary bladder, uterus, and its appendages and the dilated upper part of the rectum is normal. The lower part of the rectum is constricted, and its anterior portion is continuous with the posterior surface of the uterus, so that there is a continuous and free passage from the lumen of the rectum to the vagina and into the uterine cavity, which has a mesial septum that divides it into two cavities, each one opening freely with the corresponding fallopian tube and into the rectovaginal opening.

The posterior wall of the urinary bladder is well separated from the uterus externally, but the wall between it and the vagina is represented by a fold covered by mucosa and directed toward the urethral opening or cloacal opening, so that a probe passing through the latter could be directed into the urinary bladder, cavity of the uterus, or into the rectum.

The artificial anus is about 3 centimeters in length and communicates with the left horn of the uterus. The descending colon is dilated and contains well-formed fæces. The musculature is not hypertrophied, and the lumen measures about 7 centimeters in diameter.

The cardiovascular anomaly. The heart is dark blue and is placed transversely. The apex is blunt, and the right ventricle is more dilated, thicker, and more rounded than the left. The right auricle is more dilated than the left and contains clots of blood. The left auricle is small, especially the appendiceal portion, and the mitral orifice is also small. The foramen ovale is patent. The upper part of the interventricular septum is missing, so that both cavities empty into one common thick-walled

vessel which is bent to the left, giving at the concave portion a branch that divides into two, which are apparently the pulmonary arteries. At the convexity other branches also arise. This common vessel has three semilunar cusps, and behind the left and anterior ones the coronary arteries arise. There is a cord-like transparent tissue that has a thick center and thin ends that is fastened about the middle of the attachment of the anterior and right cusps. The upper part of the interventricular septum is concave, and anteriorly the end is between the left and right cusp and posteriorly between the posterior and left, so that two cusps are in the right ventricle and one in the left. The left iliac artery has a larger caliber than the right.

The lungs resemble the spread wings of a bird due to anomalous indentations, for the left has three lobes.

A Meckel's diverticulum is found 50 centimeters above the ileocæcal valve, which measures 3 centimeters in length and has a square blunt end.

The left kidney is elongated and has the shape of a question mark. It seems to be composed of two leaflike parts; each one has a tube which runs into a common ureter. The right is more rounded and looks like the left with the only difference that it has three parts and three tubes instead of two.

This baby died of acute gastroenterocolitis.

Autopsy 4177.—The next case is interesting, for the baby was delivered normally at the obstetrical department of the Philippine General Hospital and after two days showed symptoms of intestinal obstruction. At autopsy there were omental adhesions and marked fibrous adhesions in the peritoneal cavity that bound the coils of intestine to each other and to the peritoneum beneath the umbilicus. The coils of the lower part of the ileum are represented only by a fibrous cord, and the intestinal lumen above this is distended, while the colon has a diameter of only 4 millimeters from serosa to serosa.

GASTROINTESTINAL DISEASES

It is a known fact that infant feeding in health or in disease is one of the hardest problems that the pediatrician has to contend with and probably more so in our country where "the milk of beriberic women instead of being a blessing to the child turns to be a curse sometimes." Artificial feeding in the Philippines is difficult, for the poorer class cannot keep the milk on ice, and the temperature favors the development of bacteria in it. The time of weaning is also a period that worries the mother and the

physician because of the lack of suitable domestic infant food. Some mothers go to the extreme of long-continued nursing at the expense of their own health in order to preserve and strengthen, they say, the alimentary tract of their babies, with the result that both mother and child become rachitic. As an example of this, two years ago I was called by a middle-class family to see the youngest child, who was 1 year and 8 months old and entirely breast-fed. The parents told me that the child had an evening rise of temperature and sweating and did not thrive well; physicians had been consulted and oxypathor applied, without any result. I examined the milk of the mother, who was a multipara, and found that it was watery, and by simply giving artificial feeding, the child became well. We have also the other extreme, where young infants are fed with soft-boiled rice, bananas, and almost everything that is found on the family table.

But the worse cases are the children of the poor and ignorant mothers. If the milk is suspected to be the cause of "taol" or infantile beriberi and the mothers are advised to give two teaspoonfuls of condensed milk diluted in boiled water to their infants, they keep giving the same formula for weeks and months, with the result that the child has been probably saved from infantile beriberi to become a victim of malnutrition and finally of gastroenteritis.

Our records contain 207 cases that showed anatomically some lesion in the alimentary tract, without including those due to tuberculosis or Asiatic cholera. The most frequent associated lesions were those of the respiratory tract. Not counting tuberculosis, there were 63 cases of bronchopneumonia, 5 of lobar pneumonia, and 5 with abscesses in the lungs. The next in frequency is otitis media, 15 cases. The lesions as to location in the tract are as follows:

Acute catarrhal gastritis, 9 cases. Four of these were associated with bronchopneumonia, 1 with lobar pneumonia, 1 with chronic colitis, and still another with catarrhal duodenitis and cholecystitis in a burn case.

Gastroenteritis, 26 cases. Twelve of these were chronic and 4 associated with colitis and bronchopneumonia, 7 with bronchopneumonia, 2 with otitis media, and 1 in a male infant of 22 days associated with stomatitis.

Acute enteritis, 38 cases. Six of these were ulcerative, 1 of these being caused by typhoid, and 3 were membranous. Six cases were complicated with bronchopneumonia, 5 with tuberculosis of the lungs, 1 with empyæma, and 1 with suppurative meningitis. One had also oxyuriasis. The last is a 5-day-old

infant with subdural hemorrhage, suppurative pancreatitis, and acute choledochitis. The rest were simple catarrhal inflammations.

Acute enterocolitis, 51 cases. Thirty-seven were catarrhal, 14 of which were complicated with bronchopneumonia, 5 with otitis media, 2 with meningitis, with aspiration of food into the lungs, 1 with bronchiectatic abscesses in the lungs and empyæma, and 1 with ischiorectal abscess.

The diphtheritic type of lesion was encountered in 14 cases and the ulcerative in 3 cases. In three instances of the first and one of the latter, which was bacillary, peritonitis was found.

Chronic enterocolitis, 16 cases. Five were associated with bronchopneumonia, 2 with miliary tuberculosis, 2 with otitis media, 3 with nephritis, 1 with renal and vesical calculi, 1 with ulcerative colitis, 1 with gastric ulcer, and 1 with malaria.

Acute colitis, 33 cases. Thirteen of these were catarrhal, 10 ulcerative, 4 membranous, and 5 ulcerative and membranous. The ulcerative cases were interesting, for they were associated with different lesions, as duodenal ulcer, burn, noma, and peritonitis. Of the latter there were 4 cases, and with bronchopneumonia, 2 cases. All the ulcerative and diphtheritic cases were pure types of bacillary dysentery, 3 of which were associated with bronchopneumonia. Three of the membranous types had pneumonia and 1 tuberculous adenitis. Six cases of the catarrhal type were associated with bronchopneumonia, 1 with lobar pneumonia, 1 with omphalitis, and 2 with otitis media. One of these had also suppurative leptomeningitis. Three cases had nephritis, 1 had duodenal ulcer due to extensive burn, and 1 died due to aspiration of food into the trachea and bronchial tubes.

Chronic colitis, 34 cases. Twelve of these were catarrhal, 18 ulcerative, 3 diphtheritic, and 1 amœbic. Six cases of the catarrhal type were associated with bronchopneumonia, 3 with otitis media, 1 with pyæmia, and 1 with tuberculosis. Six of the ulcerative type had bronchopneumonia, 2 otitis media, 1 streptococcæmia, 2 tuberculosis, and 1 inguinal hernia. The description of the lesions in the amœbic colitis is not typical.

In many of these cases of gastrointestinal lesions the diagnosis of malnutrition was encountered.

OTHER PATHOLOGIC LESIONS OF THE ALIMENTARY CANAL

Ulcers in the alimentary tract of infants are not rare.

Ulcer of the œsophagus was found in a male, 1 month old, diagnosed clinically as infantile beriberi and confirmed anatomically.

Ulcer of the stomach was met in 3 instances; the first case was a male 25 days old, with the clinical diagnosis of acute gastroenteritis and marasmus and anatomic diagnosis of lobar and lobular pneumonia, acute bronchitis, acute nephritis, and emaciation. The second case was a female 1 year and 6 months old, with chronic gastroenterocolitis, and the third case had ulcerative gastritis and was tuberculous.

Duodenal ulcers, 7 cases. Two of these were due to extensive burns, 1 in a male 5 years old and 1 in a female 1 year old. There is also the record of a case of hemorrhage into the stomach and duodenum with acute bronchopneumonia.

Gall bladder. Besides the congenital anomalies and migration into the gall bladder or into its ducts of parasites, we have 6 cases of catarrhal inflammation. In 1 of these the cholera vibrio was isolated from the gall bladder, and in 2 the lesions seemed to be secondary to those found in the alimentary tract, for in one there was acute diphtheritic enterocolitis with fibrinous peritonitis, and in the other there were hepatic abscesses and tuberculosis of the gastrointestinal tract. The cause of death in 2 was burn and in 1 infantile beriberi.

Perforative diverticulitis was encountered in a boy 4½ years old with acute peritonitis and free *Ascaris* in the peritoneum.

Intestinal obstruction was found once in a girl 25 days old, due to suppurative omphalitis and acute and chronic peritonitis.

The record shows one case of intussusception in a boy 10 months old, who also had generalized tuberculosis. The lower part of the ileum with the base of the appendix formed the intussusceptum and the first part of the ascending colon the intussuscipiens. This series included also a case of megacolon with *Dipylidium caninum.*(34)

ASIATIC CHOLERA

As to age, our statistics show that Asiatic cholera attacks all ages and that it increases with age. One premature case lived for six days, and cholera vibrios were found in the intestinal contents after death. The mother of this child had symptoms of abortion for which she was taken and delivered at once in the obstetrical department of the Philippine General Hospital. Soon after delivery they found that the mother was suffering from cholera; she was sent to San Lazaro Hospital, where she died.

August and September have the highest infant mortality record due to cholera, while the record of five years shows its absence during the hot months of April and May (Table I).

TABLE I.—*Infant mortality due to cholera, Manila, 1910–1916.*

Year.	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.
1910	2	1				7	8	12	2	1	1	
1911												
1912												
1913										4	4	3
1914	4	1					7	22	26	5	2	2
1915	3	1	3									
1916		2										
Total	9	5	3			7	15	34	28	10	7	5

Our statistics show 103 cases, or 10.3 per cent. We believe that this percentage would have been higher if the intestinal contents had been examined for cholera vibrio in those cases that were diagnosed clinically as cholera infantum and anatomically as acute catarrhal enteritis, especially during epidemics.

McLaughlin,(32) after careful investigation, came to the following conclusions:

> Cholera in children is often unrecognized and unreported as such, being reported as acute or chronic enteritis, gastro-enteritis, entero-colitis, dysentery, acute or simple meningitis, and probably also as "infantile" beriberi, convulsions of children, and other diseases. * * *
>
> The clinical picture of cholera in children is often atypical, and the diagnosis may be extremely difficult if not impossible without a bacteriological examination of the intestinal contents. Cerebral manifestations in children suffering from cholera are very common and their severity is in inverse proportion to the age of the child. Acute meningitis is a very rare disease in Manila, in spite of the statistics to the contrary. The percentage of children attacked by cholera is higher than shown by the statistics of the Bureau of Health.

During this last epidemic of cholera (1916), Doctor Crowell ordered that routine examination of the intestines and gall bladders of all autopsies be made. It was found that many children that were clinically diagnosed with some intestinal trouble harbored the cholera vibrio.

TABLE II.—*Age incidence of cholera cases.*[a]

Months.	Cases.	Years.	Cases.
0 to 1	4	1 to 1½	13
1 to 2	2	1½ to 2	10
2 to 3	3	2 to 2½	15
3 to 4	0	2½ to 3	7
4 to 5	1	3 to 3½	27
5 to 6	3	3½ to 4	5
6 to 7	0	4 to 4½	16
7 to 8	0	4½ to 5	11
8 to 9	2		
9 to 10	1		
10 to 11	1		
11 to 12	1		

[a] No age given, 1 case.

In reviewing these records, one's attention is attracted by the great frequency of the association of the disease with *Ascaris lumbricoides* and their migratory activity. In 2 cases they were found in the liver, once in the appendix, twice in the gall bladder, and once in the bile ducts.

In view of the fact that almost all these patients were either taken to San Lazaro Hospital when sick or died in their homes and did not receive treatment for *Ascaris* as did those that came from the Philippine General Hospital, we cannot draw the conclusion that these parasites are one of the predisposing causes, acting either by lowering the vitality of the patient or by disturbing the function of the alimentary tract.

Concomitant anatomical lesions. Bronchopneumonia was found in 14 cases. In 6 cases of miliary tuberculosis the cholera vibrio was found bacteriologically in the intestinal contents. It is well known that the mere presence of these vibrios does not mean that the patients were suffering from cholera.(9)

INTESTINAL PARASITES

The tropical climate is a favorable one for the development of intestinal parasites, as, for example, has been demonstrated by Wharton(52) in his study of *Ascaris* eggs, who found that at room temperature ten days are sufficient to develop the freshly laid eggs into embryos. Epstein,(14) in the United States, cultivated the eggs of *Ascaris* and found that the embryo was developed after five weeks, and when fed to children, the ova appeared in the stools after three months.

In our records there are 159 cases, or 15.9 per cent, of infection of the four commonest nematodes—*Ascaris, Trichuris, Ankylostoma,* and *Oxyuris,* and only 1 case of cestode, *Dipylidium caninum,* which was reported to the Manila Medical Association on November 1, 1915.(34)

Cautley(8) cites that girls are more frequently infected than boys, but our record shows the number of boys (83) to be higher than the number of girls (76).

The migration of these worms, especially that of *Ascaris lumbricoides,* is remarkable. It was found five times in the liver, once in the appendix, twice in the gall bladder, and once free in the peritoneal cavity in a case of perforated diverticulitis.

Oxyuris was found once in the appendix in a case of tuberculous colitis.

It seems that their migratory activity is stimulated by an abnormal condition of the bowels, for in those cases where they were found in the gall bladder, liver, and appendix, the patients

died of cholera. The size of the adult parasites being greater than the ampulla of Vater or the appendiceal opening, did they go in when they were young, as believed by Perroncito,(41) has there been a previous dilatation of these ducts before their migration, or were these migrations post mortem?

This migratory activity seems also to be stimulated by hunger of the host; for during my service in the department of medicine, Philippine General Hospital, I used to treat children, and adults as well, with symptoms of peritonitis, who proved to harbor a great number of ascarides, by Murphy's peritonitis treatment and saw the subsidence of the symptoms and passage of the worms without the use of any drug.

Table III shows the kind of worms and varieties affecting individuals by age.

TABLE III.—*Age distribution of infection by worms.*

Age.	Cestode.	*Ascaris* alone.	*Trichuris* alone.	*Oxyuris* alone.	*Ankylostoma* alone.	*Ascaris* and *Trichuris.*	*Ascaris* and *Oxyuris.*	*Ascaris* and *Ankylostoma.*	*Ascaris, Trichuris,* and *Ankylostoma.*
Months.									
0 to 1									
1 to 2									
2 to 3									
3 to 4		2							
4 to 5									
5 to 6		1							
6 to 7		1	1						
7 to 8		1							
8 to 9	1	1							
9 to 10			1			1			
10 to 11		2							
11 to 12		1							
Years.									
1 to 1.5		13	1			2			
1.5 to 2		12	1						1
2 to 3		24				7	1		
3 to 4		24		1		10	2	1	2
4 to 5		30	2			13			
Total	1	112	6	1		33	3	1	3

As we see, *Ascaris* is the worm that first invades the human alimentary tract and the one that infests the most, being found alone in 112 cases, and if we include those cases where *Ascaris* was found with other intestinal parasites, the number of children infested will rise to 152, or 95.5 per cent.

Garrison and Llamas(19) found 95 per cent of children in

Manila infected with intestinal parasites. In their examination *Trichuris* was found in 92 per cent, *Ascaris* in 56 per cent, *Ankylostoma* in 11 per cent, *Oxyuris* in 1.33 per cent, and *Taenia* in 0.66 per cent.

Garrison, Leynes, and Llamas(18) give the following age distribution of children below 5 years in Taytay, Rizal Province:

TABLE IV.—*Age distribution of infections.*

Age.	Examined.	Infected.		*Ascaris.*		*Trichuris.*		Hookworm.		*Strongyloides.*	
		Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Under 2 years	73	46	63	39	53.4	22	30.1	0	------	0	------
2 to 4 years	100	96	96	87	87	75	75	1	1	2	2.0

TUBERCULOSIS

Musgrave and Sison,(37) in their study of 1,000 cases of phthisis among the Filipinos, say that the infection among children probably is much below that in adults, because many die before the first year of life and no doubt before tuberculosis has been contracted or has developed to a degree sufficient for recognition.

In this series tuberculosis has been met in 8 per cent, which is very much lower than that found by Gilman(22) and Andrews(5) in adults.

Tuberculosis in infants is highest in the second year and greatest during the first two years of life, decreasing as age advances as shown in Table V.

TABLE V.—*Age incidence of tuberculosis.*

	Cases.
Premature	1
0 to 1 month	1
1 to 6 months	3
6 to 12 months	13
1 to 2 years	17
2 to 3 years	22
3 to 4 years	12
4 to 5 years	11
Total	80

Our premature case lived for thirty-one days and had tuberculous mesenteric lymphatic glands. Whether this is acquired or is an instance of intrauterine infection, I cannot say. The

intrauterine infection, although rare, has been established according to Holt(27) by various authenticated cases and by the work of Martha Wollstein(53) on tuberculosis of the placenta. Holt mentions the case of a premature infant that lived twenty-one days, born of a mother suffering with advanced tuberculosis, whc at the autopsy showed tuberculosis of the endometrium.

The number of cases in which the different organs and lymphatic glands were affected is shown in Table VI.

TABLE VI.—*Organs and lymphatic glands affected by tuberculosis.*

Lungs	58	Jejunum	1
Cervical glands	22	Ileum	32
Bronchial glands	13	Colon	18
Peribronchial glands	38	Appendix	2
Mediastinal glands	9	Rectum	0
Mesenteric glands	42	Liver	24
Retroperitoneal glands	9	Pancreas	2
Meninges	14	Gall bladder	0
Pleura	54	Diaphragm	1
Peritoneum	7	Spleen	28
Omentum	4	Adrenal	3
Pericardium	0	Thymus	3
Ependyma	2	Thyroid	2
Joints	1	Pineal gland	1
Bones	1	Kidneys	1
Reproductive system	0	Ureter	1
Œsophagus	0	Brain	4
Stomach	1	Cerebellum	1
Duodenum	0		

Lungs. Of the 58 cases of pulmonary tuberculosis, both lungs were involved in 42. The right was singly affected eleven times, and the left was affected five times.

The type of the lesions indicates a more diffuse and acute process than in adults, and in some instances two or three different types were found. There were 23 cases that showed acute miliary tuberculosis, 10 of which were associated with cavities of the pneumonic type, 12 were lobar, and 7 were lobular.

Chronic type of lesions was found in 16 cases, although in 10 the condition was accompanied by ulcerative lesions. In only one case have I seen calcification, which was that of a girl 11 months old (autopsy 1431), who also had acute miliary pulmonary tuberculosis and otitis media.

Peribronchial lymphatic glands. If we follow Holt's(27) description, he divides these into three main groups: the first are those that surround the trachea; the second, those situated at the bifurcation of the trachea and surrounding the primary

bronchi; while the third follows the course of the bronchi into the lungs. That all these glands may be involved is shown by a case where a localized triangular-shaped tuberculous bronchopneumonia of the left upper lobe of the lung showed enlarged glands all along the course of the bronchi and caseous glands around the trachea and hilum of the left lung only.

As to the rôle played by the bronchial glands, Wollstein(53) found the glands adjacent to the right bronchus the seat of primary lesion in 74 per cent of her cases.

Rothe(45) and Dunn(12) believe that the respiratory tract is the usual entrance of the infection in children.

In this series the cervical and thoracic glands were found macroscopically tuberculous in 82 cases, the mesenteric and retroperitoneal in 51 cases, and both sets in 21 cases.

The aërogenic type of infection in Filipino children is probably also the rule, since artificial feeding with fresh cow's milk or any domestic animal is rare and since tuberculosis among cattle and hogs is reported by Brewer as absent.(7)

TABLE VII.—*Relation of involvement of different organs.*

	Cases.
General miliary	28
Lungs and thoracic lymphatic glands only	13
Lungs and mesenteric glands	2
Lungs and intestine and mesenteric glands	12
Lungs, thoracic glands, and liver	1
Lungs and meninges	1
Lungs, pleura, spleen, and thoracic glands	1
Lungs, glands, and spleen	1
Lungs, pleura, and mesenteric glands	1
Lung (left), mediastinal glands, diaphragm, and spleen	1
Lymphatic glands only	6
Intestines and mesenteric glands	4
Intestines and brain	1
Intestines and peribronchial glands	1
Jejunum alone	1
Thoracic glands and meninges	3
Bones and joints	1
Intestines, healed ulcers	1

Pleura. The pleura showed the miliary form in 8 cases and fibrosis in 42, which is the opposite to the type seen in the lungs.

Alimentary system. The ileum held the first place. The stomach case was a boy 5 years old (autopsy 2524) that died of multiple abscesses of the liver due to *Ascaris* and ulcerative tuberculosis of the stomach and intestines.

The liver, spleen, and kidneys were affected in the miliary form, especially the last, or were also involved in a general

pulmonary tuberculosis. This also is true of the pancreas, adrenals, thymus, thyroid, pineal gland, omentum, and peritoneum.

Only 2 cases of tuberculosis of the brain and meninges were associated with pulmonary tuberculosis, all the rest being accompanied by general miliary tuberculosis. In one of these there was a solitary tubercle in the middle lobe of the right lung with caseous peribronchial and tracheal glands.

Causes of death by age. First year. General miliary tuberculosis, 8 cases; pulmonary tuberculosis, 9 cases; bronchopneumonia, 1 case; beriberi, 1 case.

Second year. General miliary tuberculosis, 11 cases; malaria 2 cases; colitis (bacillary) and bronchopneumonia, 1 case; pyæmia, 1 case; status lymphaticus, 1 case; confluent bronchopneumonia, 1 case; pulmonary tuberculosis, 2 cases; and 1 of cancrum oris. One case of general miliary tuberculosis died of cholera, and 1 case of malaria had tuberculosis of the intestine.

Third year. General miliary tuberculosis, 4 cases; burn, 1 case; intestinal tuberculosis, 2 cases; cholera, 3 cases; postoperative (otitis media), 1 case. The last one died of lobar pneumonia and bronchiectatic abscesses of the lungs, the tuberculous ulcers in the intestines having healed when the body came to autopsy. One of the cases of intestinal tuberculosis had a solitary tubercle in the cerebellum.

Fourth year. Generalized miliary tuberculosis, 4 cases; pulmonary tuberculosis, 3 cases; suppurative peritonitis, 1.

Fifth year. Three cases, due to pulmonary tuberculosis, abscess of the liver, and tuberculous meningitis, respectively.

INFANTILE BERIBERI

In 1908 infantile beriberi among Filipino infants was confirmed by autopsy,(3) and since the studies on infant mortality of McLaughlin and Andrews,(33) the monograph of Guerrero and Quintos,(25) and the experiments of Andrews,(4) this infantile disease has been accepted as an entity.

Infantile beriberi has been for many years at the head of the list of the causes of infant mortality in Manila. The report of the Philippine Health Service for 1915(43) shows that this disease needs a more careful consideration.

As to its etiology, the local physicians attribute it to the milk of the nursing woman, who is either suffering from beriberi or has it in a latent form.

Andrews(4) thinks that the disease is not due to bacteria in the milk nor to toxins, for the anatomical findings do not agree with any of them, and sustains the former view(33) that milk is

deleterious because of something it lacks rather than because of any harmful constituent. He further states that that something which is lacking is needed for the growth and development of nerves and that beriberi is a nutritional disease.

Darling,(16) in 1914, showed the intimate relationship between scurvy and beriberi in adults as to its etiology and that these and certain other cachexias are the result of the continued use of one-sided and deficient diet.

Hess,(26) in his studies of infantile scurvy in children fed with boiled milk, found that the symptomatology and pathology of this assumes actual relationship to beriberi, which is emphasized by a dietetic test modeled after the tiqui-tiqui treatment of infantile beriberi. He used middlings, the pericarp of wheat.

Beriberi in adults has been reported by Little(30) from countries where rice is not used for diet. Signs of beriberi in puppies were produced by feeding them with beriberi milk by Andrews.(4) Neuritis was produced by Gibson(20) in birds by feeding them with normal human milk along with polished rice, and infantile scurvy by Hess(26) in children by using boiled milk.

Poverty and the so-called deficiency diseases are found in many places, and yet infantile beriberi is met only in beriberi regions. This seems to indicate that the disease is prevalent only in infants nursed by women with an exclusive diet of rice (Well and Mouriquand).(51) If this is not so, can we get the same good results by using middlings, or the extract of tiqui-tiqui, or vice versa, in treating infantile scurvy or infantile beriberi?

Vedder(50) believes that the neuritis-preventing substance is probably an organic base as claimed by Funk and showed that it is not volatile and is destroyed by heat.

Fraser and Stanton(15) and later Grijns(24) also demonstrated that heat destroys the protective power of unpolished rice. Can we produce infantile beriberi by feeding healthy infants with the heated milk of nursing women whose diet is other than unpolished rice or can it be produced by the heated milk of healthy women on exclusive rice diet?

Ingier(28) succeeded in producing scurvy in pregnant guinea pigs by following Holst and Frölich's diet and was able to transmit the disease to their offspring. This experiment is in accord with the experience of the local physicians of the preventive value of changing the rice diet of the pregnant or nursing woman with symptoms of beriberi for mongo, rice polishing, or bread.

But those cases that do not show any symptom of beriberi

during pregnancy or the nursing period and yet in which we see the attacks of infantile beriberi in their offspring or nurslings seem to contradict the findings of Ingier and Goldmann(28) in their experiments. The first found the lesions of scurvy more marked in the skeleton of the mother than in the offspring.

Seasonal prevalence.—Table VIII shows that infantile beriberi is more prevalent in September, October, and November, disappearing gradually with the approach of the hot season (April, May, and June), according to Andrews.(4) Our records between January, 1910, and March, 1916, show the following annual and monthly incidence:

TABLE VIII.—*Annual and monthly incidence of infantile beriberi.*

Month.	1910	1911	1912	1913	1914	1915	1916	Total.
January	12			1	1			14
February	35		1				1	37
March	29			2				31
April	11							11
May				1				1
June		1						1
July			1		1	1		3
August	7	3			1			11
September	1	3		1	1			6
October		4	1	2	2	1		10
November		6	2	7		2		17
December		3	2	3		1		9
Total	95	20	7	17	6	5	1	

As we can see, the only months that are more or less exempted are May, June, and July, which are the beginning of the rainy season and the time when palay, or rice, is planted.

The annual occurrence is not the same, and Albert(2) thinks that this may perhaps be explained by the lack of vitamines in certain foods that is observed in certain periods due to agricultural and economic causes.

If the record of 1910 is not taken, but only those of the following years, the monthly incidence is completely different, and we have January, 2; February, 1; March, 2; April, 0; May, 1; June, 1; July, 3; August, 4; September, 5; October, 10; November, 17; and December, 9; which gives the highest mortality during the wet, moist, and cold months. The infrequency of infantile beriberi of these last years may be due to the fact that even the laity is aware of its symptoms, and artificial feeding is given at once.

TABLE IX.—*Age incidence of infantile beriberi cases.*

	Cases.		Cases.
0 to 1 month	6	8 to 9 months	3
1 to 2 months	56	9 to 10 months	1
2 to 3 months	44	10 to 11 months	2
3 to 4 months	12	11 months to 1 year	0
4 to 5 months	6	1 to 1.5 years	2
5 to 6 months	10	2 years and 7 months	1
6 to 7 months	4	Unknown	1
7 to 8 months	2		
		Total	150

It is plainly shown that the highest incidence is in the first three months of life. The oldest case (autopsy 2869) is that of a girl 2 years and 7 months old; the pathologist (B. C. Crowell) wrote the following note: The hypertrophy and dilatation of the heart was due to infantile beriberi, this being probably a residual of an infantile condition.

Of these 15 cases, 65 cases were clinically diagnosed as infantile beriberi and confirmed at autopsy. The clinical diagnosis of the rest is worthy of note, for almost all of them gave symptoms suspicious of either cerebral or respiratory trouble.

Convulsion, 25 cases; meningitis, 3 cases; eclampsia, 2; acute bronchitis, 25; diphtheria (?), 2; bronchopneumonia, 5; undetermined, 10; no diagnosis, 9; nephritis, 1; chronic gastritis, 1; and status lymphaticus, 1. During my hospital service in pediatrics I was more than once tempted, from the clinical standpoint, to diagnose infantile beriberi as status lymphaticus.

Associated anatomicopathologic lesions. Cholera, 1 case; hyperplasia of the spleen, 6; hyperplasia of the glands, 5; hyperplasia of the thymus, 4; acute nephritis, 3; cloudy liver, 2; cloudy kidneys, 1; patent ductus arteriosus, 2; bronchopneumonia, 1; acute suppurative bronchitis, 1; patent fossa ovalis, 3; cystic ovaries, 1; emphysema, 1; ulcerative colitis, 1; tuberculosis, 1; and enterocolitis, 1.

Pure types of infantile beriberi, that is, dilatation and hypertrophy of the right ventricle of the heart, subserous petechial hemorrhages, more or less œdema of the lungs and congestion of the visceral organs, and subcutaneous and serous transudation of fluid, were present in 132 cases.

The hypertrophy and dilatation of the heart has been a perplexing point to almost all the workers in this disease. According to the transactions of the Second Regional Assembly of Physicians and Pharmacists in the Philippines,(1) Guerrero and

others believe that the degeneration of the vagus nerve is the cause of the cardiac dilatation. Albert thinks that the increase of tone of the vagus or its abnormal irritability is the immediate cause of the hypertrophy and dilatation of the right ventricle, while Villareal mentioned that in Japan Miura laid great emphasis on the increase of the second pulmonic sound in diagnosing cases of beriberi.

Miura(35) explains the condition of dilatation-hypertrophy of the right heart in beriberi as due to a diminution in the mass of the lungs through the raising of the diaphragm and the contraction of the ultimate branches of the pulmonary artery through the action of the beriberi poison; Yamagiva,(54) to the contraction of the pulmonary arterioles. Ogata(38) states that there is no diminution of the lumen of the pulmonary vessels in the said disease, and that, if there is any contraction of these vessels, it is only due to post-mortem rigidity.

Matsuoka,(31) in 1911, studied the pulmonary œdema in beriberi and came to the conclusion that in that disease the condition is due to an early weakening of the left ventricle and that the hypertrophy of the right ventricle found in beriberi favors the raising of the pressure in the pulmonary artery and the occurrence of pulmonary œdema. Later in 1915 the same author, after an exhaustive work on changes in the lungs in beriberi, came to the following conclusions:

1. Although pathognomonic pictures of beriberi lungs are still wanting, they have the following characteristics:
   a. Diminished air capacity or collapse (in spite of vicarious emphysema in one part), and following generally upon this small volume and sharp margins.
   b. Especially important is the congestion-œdema; this is not confined to the agonic period, in which there may be paralysis, but a true congestion-œdema. Heart-failure cells are to be found not infrequently. Distinct splenisation is present in marked cases of beriberi.
2. The above-mentioned œdema is of constant occurrence, in many areas circumscribed or diffuse.
3. Besides the ascent of the diaphragm following on paresis, there exist for the explanation of the collapse (of varying degrees) numerous important factors, of which hydrothorax is perhaps the most important.
4. For the setting up of dilatation and hypertrophy of the right heart, congestion and congestion-œdema must work hand in hand with the collapse.

Tadaharu Maruyama(48) thinks that the cause of the nerve and muscle degenerations is probably some poison of the existence of which there is as yet no proof.

Hess(26) believes that the pathogenesis of the cardiac enlarge-

ment in scurvy is an involvement of the vagus and that it is hard to understand the predisposition of the right heart to enlarge unless this is associated with a disturbance of the circulation in the lungs. He mentions also the frequent occurrence of pneumonia in the course of scurvy.

In this series bronchopneumonia was diagnosed as terminal and slight in two cases of infantile beriberi (autopsies 1616 and 1618), and description of the lungs is as follows:(4)

> Scattered over the surface are a few darker colored areas which are slightly firmer on section, are not elevated above the surface, do not appear granular, and on slight pressure considerable edema fluid can be expressed.

BRONCHOPNEUMONIA

Disease of the respiratory tract is second in rank in the causes of infant mortality in Manila and first in other big cities (Albert).(2)

This vulnerability or weakness is, according to Holt,(27) due to its structure, for the trachea of the young is relatively larger, the bronchi are more numerous and occupy greater space, the air sacs are much smaller, and the interstitial tissue is more abundant; besides that, the capacity of the thorax is encroached upon by the high position of the diaphragm, the large size of the thymus gland, and the frequent distention of the stomach and intestines.

The seasonal and age incidences in this series, which comprises 180 cases, or 18 per cent, without including tuberculosis, is as follows:

TABLE X.—*Seasonal incidence of bronchopneumonia cases.*

Month.	1910	1911	1912	1913	1914	1915	1916	Total.
January		2	3	1	8	4	7	25
February	1	0	3	3	2	4	6	19
March	4	0	3	2	4	2	4	19
April	3	0	3	1	3	0		10
May	0	1	0	1	1	2		5
June	0	5	3	1	1	1		11
July	4	3	2	3	3	1		16
August	3	1	4	3	6	1		18
September	0	1	1	2	6	3		13
October	0	5	5	5	1	1		17
November	0	5	3	6	0	0		14
December	0	2	3	3	2	3		13
Total								180

TABLE XI.—*Age incidence of bronchopneumonia cases.*

	Cases.
0 to 1 month	21
1 to 6 months	55
6 months to 1 year	38
1 to 2 years	35
2 to 3 years	17
3 to 4 years	9
4 to 5 years	5
Total	180

The above tables show that the mortality is less during May and that the disease is prevalent throughout the year. They also show that the younger the patient the more fatal is the disease and that its occurrence diminishes inversely with age, which is in accord with textbooks.

The sexes in the series are not equally affected, the male sex predominating, there being 100 males and 80 females.

Seat of lesions. Bronchopneumonia is usually bilateral and is found frequently in the posterior parts of the lungs and many times in the lower lobes. In this series the right lung was singly affected in 23 cases and the left in 12 cases. The left lower lobe is the first in the order of frequency, followed by the lower lobe of the right, then the upper lobe of the same side, and lastly the upper lobe of the left. The middle lobe of the right was found affected alone in one instance.

Associated pathologic lesions. Bronchopneumonia is in many instances terminal, and at autopsy it is not always easy to decide accurately whether the lung lesion preceded the other lesions, as those of the alimentary tract, marasmus, and meningitis, or whether it was secondary to them. This type of lung lesion was found associated with some form of morbid condition of the alimentary tract in 90 cases, 12 being Asiatic cholera, and 2 acute enteritis due to typhoid. Some of these were accompanied by other lesions, as otitis media, 5 cases; fibrinous pleurisy, 4; suppurative meningitis, 1; catarrhal cholecystitis, 2; renal and vesical calculi, 1. Other cases showed 2 or 3 morbid conditions, as otitis media; ulcerative colitis and noma or otitis media; and colitis and chronic leptomeningitis.

As extension downward from diphtheritic tracheobronchitis there were 5 cases, and as extension from some pathologic lesion in the other parts of the lungs, as lobar pneumonia and abscesses, there were 12 cases.

It was also found in 2 cases of pyonephritis, in 5 cases of

meningitis, in 19 cases of otitis media, and in 8 cases of abscesses located in different parts of the body.

Parish(39) points to the following factors as causes of the prevalence of respiratory affections among Filipino children.

1. Lack of proper clothing.
2. Lack of protection while sleeping.
3. Cold baths usually taken outdoors, under the faucet many times without drying or friction, thus subjecting the child to shock and chilling.
4. Untreated pertussis and other specific bronchial trouble.
5. Infantile beriberi with deficient heart action.
6. Tachycardia which seems to be the rule among Filipinos. Many of these cases suffer from dyspnœa, perspire easily and very profusely, and are easily affected by drafts.

To these I will add the custom of wrapping the newly born infant with flannel or cotton cloth and not bathing the child until after the first or second months. In some instances bath is given, and in these cases tepid water is used until they are 2 or 3 years old.

LOBAR PNEUMONIA

The anatomic diagnosis of lobar pneumonia was found in 36 cases only.

The age incidence does not correspond with what is expected, that frequency is in direct proportion with age.

TABLE XII.—*Age incidence of lobar pneumonia cases.*

	Cases.
0 to 6 months	11
6 months to 1 year	5
1 to 2 years	10
2 to 3 years	3
3 to 4 years	5
4 to 5 years	2
Total	36

The youngest is a female 22 days old that had lobar pneumonia of the right upper and inferior lobes. The clinical diagnosis of this was infantile beriberi. Next a male and a female, each 25 days old, both showing acute parenchymatous nephritis.

There is only one case that had pneumonia alba and in whose liver *Treponema pallidum* was demonstrated by Levaditi's method of impregnation. The child was a female 3 months old that died of chronic hemorrhagic internal pachymeningitis.

Site of lesion. The left lower lobe was singly affected in 10 cases, and the left upper was affected only once. The right upper

lobe was affected four times and the lower only once. Combined lesions: The right upper lobe has the most varied combinations—with the left lower lobe twice, with the right middle three times, and with the posterior of the right lower lobe and with the right lower lobe once each. The lower lobes and the right middle were involved only once. As we see, the right middle lobe was not singly affected, but only as an extension from the other lobes of the same side.

Our order of frequency is: Left lower lobe thirteen times; right apex, ten times; right base, five times; left apex and the middle, three times per extensionem. This corresponds with that of Holt.(27)

Freer(16) gives this order of frequency—upper lobes are affected as frequently as the lower: More frequently the right upper and the lower left, the former at least twice as often as the right lower; quite frequently also the middle lobe; not uncommonly both lungs involved. During the first years of life, the upper lobes are more often attacked.

Associated lesions. There were 13 cases with serofibrinous pleurisy, 1 with suppurative pericarditis, and 1 with empyæma. It was associated with some form of gastrointestinal trouble in 15 cases, of Asiatic cholera in 4 cases. One had diphtheria, and in another there was found thrombosis of the longitudinal and lateral sinuses of the head. Five cases had also bronchopneumonia, 3 meningitis, 1 empyæma, and 1 otitis media. The records of 4 cases show hypertrophy and dilatation of the heart, 2 of them being clinically diagnosed as infantile beriberi.

One case had bronchiectic abscesses and suppurative anterior mediastinitis with noma. Two cases had empyæma in the same side as the pneumonic lobe, which was the left lower.

MENINGITIS

Meningitis has been a favorite clinical diagnosis in cases dying of convulsion, for frequently the physician is only summoned to see the infant in his last hours, or because many of the diseases of these young beings have a hidden and rapid course.

Our record shows 42 cases, the male sex surpassing the female in number, there being 25 of the former and 17 of the latter. The age incidence shows that even the very young can be affected. The youngest is a 5-day-old female with sacral spina bifida, and the next is another female with ectopia vesicæ, that lived for eight days.

TABLE XIII.—*Age incidence of meningitis cases.*

	Cases.
0 to 1 month	3
1 to 6 months	6
6 to 12 months	9
1 to 2 years	10
2 to 3 years	5
3 to 4 years	5
4 to 5 years	4
Total	42

Types. Tuberculous meningitis is the most frequent type as a rule; yet our record shows 22 cases of suppurative, 16 of tuberculous, and 3 of hemorrhagic pachymeningitis and 1 of chronic leptomeningitis.

The diagnosis of suppurative meningitis has been made many times upon the gross pathological lesions and was found in infants of less than 1 year, except in one instance, and also up to the second year, except in three cases. This finding is in accord with Zappert.(55)

Associated pathological lesions. All the cases of tuberculous meningitis were the result of an extension of a generalized miliary tuberculosis, except two, which were associated with pulmonary and glandular tuberculosis.

The suppurative form was associated with bronchopneumonia in 6 cases; in 2 with lobar pneumonia, and in 6 with otitis media; 2 of these were hemorrhagic. The rest had no other recorded marked lesion.

TYPHOID FEVER

Although typhoid fever is met with great frequency in adults in Manila, yet this series shows only 3 cases. The youngest is a male infant, 7 months and 20 days old, that had swollen Peyer's patches in the upper part of the ileum; these became pronounced, larger, hemorrhagic, and ulcerated as one approached the ileocæcal valve. The solitary lymph follicles were not involved. The spleen was enlarged and soft with increased splenic tissue. The second is a 1-year-old female that had bronchopneumonia, swollen Peyer's patches, enlarged and soft glands, and hyperplasia of the solitary lymph follicles. The intestinal contents were watery and yellowish. The spleen was enlarged, dark colored, and soft. The third is a 5-year-old male with mesenteric lymphadenitis and swollen Peyer's patches.

From this we see the infrequency of typhoid in children below 5 years of age, although Rogers(44) speaks of its frequency in children of India. Domingo(11) found no case under 2 years

and only one from 2 to 5 years in his clinical report of 27 hospital cases.

Typhoid in children has a mild course, and Percy,(40) in his clinical report of 380 cases, did not see any perforation.

Fœtal typhoid has not been reported in Manila as far as we know. The study of Morse(36) is nevertheless worthy of note. He comes to the following conclusions:

> Infection of the child from the mother is a frequent, but not an invariable occurrence. The bacilli may pass directly from the maternal into the fœtal circulation. The fœtal form of disease is a general blood infection since the intestines are not functionally active. The most common result is death of the foetus and consequent abortion; but the child may be born alive still suffering from infection and die in a short time because of its feeble resistance. Whether a foetus may recover completely and be born alive and well is not yet established.

Griffith and Ostheimer,(23) in 302 cases of typhoid in children under 2½ years of age, found 2 cases of perforation.

MALARIA

In spite of the fact that malaria is prevalent in the tropics and is met with in pregnant women of the Philippine General Hospital,(49) we have no record of an intrauterine infection.

The pathological lesions were similar to those found in adults. In this series 6 cases are found; the youngest is a girl 1½ years old.

TUMORS

Six cases of tumors are found in this series: 2 cases of glioma of the eye, 1 of fibromata of the capsule of the liver (autopsy 2057), 1 of adenoma of the intestine, and 1 of neuroblastoma of the adrenal, which was diagnosed macroscopically as tuberculosis. Autopsy 1538 shows enlargement of the pineal gland, measuring 15 by 10 by 3 millimeters, which presses upon the aqueduct of Silvius. In the wall of the intestine is noticed a small grayish red area 1 by 0.5 by 0.5 centimeter, which is firm, and section shows a glistening grayish red surface and definite cellular structure. Beneath the endocardium of the heart, more especially on the left than the right ventricle and also in the muscular wall of the left ventricle, are noticed a few small, firm grayish white areas.

Histological examination shows adenoma of the intestine and œdematous myoma of the heart. (B. C. Crowell.)

SUMMARY

This study on the anatomicopathologic lesions of Filipino children under 5 years shows that:

(1) Hemorrhage is the most frequent cause of death during

the first few days of life and that the brain and meninges are the favorite seats. Congenital anomalies are also responsible in many instances.

(2) Of the children in this series 15.9 per cent are infected with nematodes, and the frequency of infestation increases as age advances. The first variety that invades the alimentary tract of children and the one that infects the most is *Ascaris lumbricoides,* 95.5 per cent. This worm shows also a great migratory activity, which is probably favored by an abnormal condition of the intestines.

(3) The most frequent concomitant lesion of gastrointestinal disease is bronchopneumonia. In 193 cases the morbid condition was located in the colon in 68 and in both intestines in 54 cases. Amœbic dysentery is very rare in children, there being only one recorded case, and yet the lesions as described are not typical.

(4) Asiatic cholera was nil during April and May, the incidence increasing with age and during epidemics. Newly born infants can be infected during their existence from a mother suffering with the disease.

(5) In infants it is almost the rule for tuberculosis to become generalized rather than localized, the lungs being the commonest seat of lesion and the aërogenic type the most frequent mode of infection. The pericardium, œsophagus, duodenum, rectum, gall bladder, and reproductive system were not affected in this series even in a generalized acute and diffuse infection. Tuberculosis in this series has been found in 80 casés.

(6) Infantile beriberi has been anatomically diagnosed in 150 cases. The literature shows that the disease is met only in infants born of, or nursed by, women on an exclusive rice diet. It is not seen in Manila in the children of foreigners that do not eat much rice. If the neuritis-preventing substance is destroyed by heat, can we produce infantile beriberi by feeding healthy infants with heated milk of nursing women whose diet is other than polished rice or can it only be produced by the milk of healthy women who live exclusively on polished rice?

(*a*) If the anatomic findings of infantile scurvy are similar to those of infantile beriberi and good results can be expected by the use of middlings in the first and tiqui-tiqui in the latter, would we get the same good results if we change the treatment?

(*b*) The experiments on scurvy by Ingier and by Goldmann and the findings of Gibson and Concepcion (21) seem to be contradicted by the explanation given by some Japanese and local students of infantile beriberi that the beriberi-preventing prin-

ciple does not pass to the milk to be used by the beriberi infant, which on that account develops the disease, while it is used up by the nursing woman, who does not show any symptoms of beriberi.

(*c*) This series shows that infantile beriberi is less prevalent during April, May, June, and July and that the age most affected is between 1 and 3 months.

(*d*) The œdema-congestion of the lung pronounced by Matsuoka as the cause of the dilatation-hypertrophy of the right ventricle offers a new field of investigation in both infantile beriberi and infantile scurvy.

(7) Pneumonia, lobar and lobular, has been met with in 21.6 per cent of this series. If in this we include other diseases of the respiratory tract, we shall probably see that this tract is the most vulnerable place in young children.

(8) Suppurative meningitis has been met with more frequently in the records than tuberculous meningitis and more so during the first two years of life.

(9) Typhoid, malaria, and tumors are rare in children of this series.

(10) The pathological study of this series includes only the causes of stillbirths, of death below the first six days of life, diseases of the gastrointestinal tract, tuberculosis, pneumonias, meningitis, typhoid, malaria, and tumors.

I heartily appreciate the valuable advice and assistance given me by Dr. B. C. Crowell in the study of this series.

REFERENCES

(1) Actas Memorias y Comm. de la II Asamblea Regional de Medicos y Farmaceuticos. Tipografia Sto. Tomas (1914).
(2) Albert, Jose. *Bull. Manila Med. Soc.* (1910), 2, 286.
(3) Idem. *Phil. Journ. Sci., Sec. B* (1908), 3, 343.
(4) Andrews, V. L. Ibid. (1912), 7, 67.
(5) Idem. Cited by Musgrave and Sison.
(6) Bland-Sutton. Tumours Innocent and Malignant. 5th ed. Cassell and Company, Limited (1907).
(7) Brewer, I. C. *Phil. Journ. Sci., Sec. B* (1910), 5, 331.
(8) Cautley, E. The Diseases of Infants and Children. 1st ed. Shaw and Sons, London (1910).
(9) Crowell, B. C. *Phil. Journ. Sci., Sec. B* (1914), 9, 361.
(10) Darling. *Journ. Am. Med. Assoc.* (1914), 63, 1290.
(11) Domingo, E. Actas, Memorias y Comm. de la II Asamblea Regional de Medicos y Farmaceuticos. Tipografia Sto. Tomas (1914).
(12) Dunn, C. H. *Am. Journ. Dis. Child.* (1916), 11, 85.
(13) Editorial. *Journ. Am. Med. Assoc.* (1915), 65, 1031.
(14) Epstein. See 27.
(15) Fraser and Stanton. See 21.

(16) FREER, E. See 42.
(17) FINKELSTONE, B. B., and ELLIS, T. L. *Journ. Am. Med. Assoc.* (1915), **65**, 2155.
(18) GARRISON, LEYNES, and LLAMAS. *Phil. Journ. Sci., Sec. B* (1909), **4**, 207.
(19) GARRISON and LLAMAS. Ibid. (1909), **4**, 185.
(20) GIBSON, R. Ibid. (1913), **8**, 469.
(21) GIBSON, R. B., and CONCEPCION, I. Ibid. (1916), **11**, 119.
(22) GILMAN, P. K. Ibid. (1908), **3**, 211.
(23) GRIFFITH and OSTHEIMER. *Am. Journ. Med. Sci.* (1905), **130**, 581.
(24) GRIJNS. See 21.
(25) GUERRERO, M. S., and QUINTOS, J. El Beriberi en los Niños de Pecho. Imp. Lorenzo Cribe, Manila, I. F. (1910).
(26) HESS, A. T. *Journ. Am. Med. Assoc.* (1915), **65**, 1003.
(27) HOLT. Diseases of Infancy and Childhood. 5th ed. Appleton and Company, New York and London (1910).
(28) INGIER and GOLDMANN. See 13.
(29) KNOPFELMACHER, W. See 42.
(30) LITTLE, J. M. *Journ. Am. Med. Assoc.* (1914), **63**, 1287.
(31) MATSUOKA, Y. *Journ. Path. & Bact.* (1915), **20**, 53.
(32) MCLAUGHLIN, A. J. *Phil. Journ. Sci., Sec. B* (1909), **4**, 363.
(33) MCLAUGHLIN, A. J., and ANDREWS, V. L. Ibid. (1910), **5**, 162.
(34) MENDOZA-GUAZON, M. P. Ibid. (1916), **11**, 19.
(35) MIURA, M. See 31.
(36) MORSE. See 27.
(37) MUSGRAVE and SISON. *Phil. Journ. Sci., Sec. B* (1910), **5**, 313.
(38) OGATA, T. See 31.
(39) PARISH, REBECCA. *Bull. Manila Med. Soc.* (1910), **2**, 247.
(40) PERCY, K. G. *Boston Med. & Surg.* (1915), **173**, 565.
(41) PERRONCITO. *Le Monde Medical* (1916), Año 26, n. 517, 266.
(42) PFAUNDLER and SCHLOSSMANN. The Diseases of Children. J. B. Lippincot Company, Philadelphia and London (1908).
(43) Report of the Phil. Health Service (1915).
(44) ROGERS. Castellani and Chalmers' Manual of Tropical Medicine. 2d ed. William Wood & Co., New York (1913), 1057.
(45) ROTHE. *Deutsch. Med. Wochenschr.* (1911), **37**, 343.
(46) SCHLOSS, O. M., and COMMISKEY, L. J. J. *Am. Journ. Dis. Child.* (1911), 275.
(47) SHAW, H. L. K., and WILLIAMS, FRANK J. *New York State Journ. Med.* (1915), **15**, 348.
(48) TADAHARU MARUYAMA. Trans. XVIIth Intern. Congr. Med. London (1913), Ser. 3, pt. 2, 81.
(49) TOLENTINO, M. *Rev. Filipina de Med. y Farm.* (1914), **5**, 1.
(50) VEDDER, E. B. *Phil. Journ. Sci., Sec. B* (1912), **7**, 415.
(51) WELL, E., and MOURIQUAND, G. *Lyon Medical* (1916), **125**, 177. Abstract from *Journ. Am. Med. Assoc.* (1916), **67**, 473.
(52) WHARTON, L. D. *Phil. Journ. Sci., Sec. B* (1915), **10**, 19.
(53), WOLLSTEIN, M. *Arch. Int. Med.* (1909), **4**, 221.
(54) YAMAGIVA, K. See 31.
(55) ZAPPERT. See 42.

BACTERIOLOGIC INVESTIGATION OF FÆCES AND BILE OF CHOLERA CASES AND CHOLERA CARRIERS

By B. C. Crowell and John A. Johnston

(From the Department of Pathology and Bacteriology, University of the Philippines, and the Biological Laboratory, Bureau of Science, Manila)

The most important advance in the study of cholera within the past decade has been the recognition of the existence of carriers of the disease. These carriers are individuals who harbor the cholera vibrio while in apparent health; they are of two kinds—"convalescent carriers," who have recovered from an acute attack of the disease, and "contact carriers," who have never had the disease, but have contracted the infestation from contact with others who harbored the organism.

Table I shows the cholera cases and the cholera carriers that have been detected in Manila during the last three years.

Table I.—*Cholera cases and cholera carriers in Manila in three years.*

Year.	Persons examined.	Carriers detected.		Cholera cases.	Cholera deaths.
		Number.	Per cent.		
1914	37,160	530	1.42	490	272
1915	10,440	43	0.41	66	44
1916	243,974	1,643	0.67	1,340	513

In Bilibid Prison there was a daily average of about 2,700 prisoners during 1914. Fifty-two cases of cholera with 6 deaths occurred, and 189 carriers were detected; of the 189 carriers, 5 developed the disease in from four to eighteen days after having been detected as carriers.

As in typhoid fever the carrier state in cholera has been shown to be intimately, if not causally, related to the existence of gall bladder infection. Until very recently it has been considered that the infection in cholera was limited to the intestinal tract. It is true that as long ago as 1848 Pirogoff(37) described pathologic conditions in the gall bladder in cholera, but the importance of this was not recognized.

The next step was the recognition of the presence of the cholera vibrio in the bile in cholera cases, which has been recorded by numerous workers since 1884. Among these workers may be mentioned Doyen,(6) Kelsch and Vaillard,(27) Nicati and

Rietsch,(32) Tizzoni and Cattani,(44) Rapchevski,(38) Rekowski and Dzierzgowski,(39) Sawtschenko,(40) Girode,(8) Bruloff,(3) Defressine and Cazeneuve,(5) Kulescha,(29) Greig,(9) and Schöbl.(42) The last three authors have especially emphasized the importance of these findings.

In 430 autopsies on cholera cases Kulescha(29) found cholecystitis forty-two times (10 per cent). In 1908, in 109 cholera cases, he found the vibrio in the gall bladder forty-nine times (46 per cent), and in 1909, in 50 cases, he found it thirty-eight times (76 per cent). Bruloff(3) found the vibrio in the bile of 76 per cent of the cases examined. In 1913 Greig(9) examined the bile in 271 fatal cases of cholera and cultivated the cholera vibrio from 80 of these cases (29.5 per cent). He found naked-eye changes in the gall bladder in 12 of this series (4.4 per cent) and in 10 of the 235 cases (4 per cent) in the post-mortem records at the Medical College, Calcutta. Schöbl(42) found cholera vibrios in the bile of 17 of 39 cholera cases examined (43.5 per cent).

In our own series the cholera vibrio was isolated from the bile in 137 of 212 cholera cases (65.2 per cent) and from the bile when the intestinal contents were negative in 12 cases (5.7 per cent). In 32 cases of cholera carriers detected post mortem we found the cholera vibrio in the bile in 24 cases (75 per cent) and in the bile when the intestinal contents were negative in 14 cases (43.7 per cent).

This finding of ours appears to be important. The fact of the presence of the vibrio in the bile in so large a proportion (65.2 per cent) of cholera cases confirms and extends the work of others. The fact of finding the vibrio in the bile in so many cholera cases(12) when it could not be isolated from the intestine emphasizes the importance of examining the bile as well as the intestinal contents of all suspected cholera cases. This importance is still further emphasized by our finding the vibrio in the bile in 75 per cent of cholera carriers and in the bile alone in 43.7 per cent of 32 carriers.

The detection of cholera carriers after death by such examinations is to be expected in view of the large number of such individuals known to exist where cholera is extant. The presence of the vibrio in the bile in a larger proportion of cholera carriers than in the intestine renders the routine examination of the bile as well as the intestine in all cases where cholera is extant of greater importance. The possibility of detecting carriers in this way, who might otherwise have escaped attention, before the outbreak

of an epidemic may be of value to public-health officials in serving to localize an infected focus and allow intensive sanitary measures to be applied to the place.

There are several possibilities concerning the route by which the vibrio reaches the bile from the intestine. In 1913 Greig(12) claimed to have recovered the comma bacillus from the urine of 8 out of 55 cholera cases examined. From this finding he argued that in these cases the disease was a septicæmia. In 1914(14) he adduced further evidence to show that the disease is at times a septicæmia by isolating the organism from almost all the organs in different cases after death. In a later article(15) he refers to the probable dissemination of the vibrio in the tissues in cholera through the lymph stream rather than through the blood stream. Kulescha(29) also believed that the bile infection was of hæmotogenous origin. In 5 cases Schöbl(42) failed to confirm Liefschütz-Jakowleff's finding of vibrios in the tissues of a stillborn child whose mother had suffered from cholera. In 1910 Kulescha(29) investigated the urine of numerous cholera cases and failed to find the vibrio. In the same way Schöbl failed to find the vibrio in the urine in 41 examinations of 27 patients and convalescents. While the evidence is conflicting, it must be admitted that occasionally the disease may be a septicæmia, but that under ordinary conditions the gall bladder is more probably infected through the bile ducts from the duodenum. A few attempts on our part to isolate the cholera vibrio from parts of the body outside the intestine and bile passages have failed.

Küster and Günzler(30) note that Goldman had pointed out that charcoal fed by mouth could be recovered through a cholecystectomy wound. Küster and Günzler fed charcoal every two hours for a day before operation and after cholecystectomy recovered the charcoal from the bile.

Kulescha(29) recovered the vibrio from the bile in one case one year after the acute attack. The International Sanitary Conference at Paris(22) in 1911 reported that the duration of the excretion of cholera vibrios by cholera carriers is as a rule short (two to three weeks), but exceptionally it lasts to twelve months. It was also reported that the excretion is also intermittent and irregular and that there occur vibrio-free intervals up to twenty-one days. The occurrence of these vibrio-free periods in cholera carriers is probably accounted for by the retention of the vibrios in the gall bladder and their irregular release. At times they may be too few in the fæces to be recovered, as they are overgrown by other organisms. This irreg-

ularity not only makes it impossible to detect all carriers in any general bacteriologic survey, but it renders difficult the problem of how long a carrier should be hospitalized or regarded as a potential source of infection. Schöbl states that the administration of bile may facilitate the search for cholera carriers among quarantined persons.

Of 189 carriers detected in Bilibid Prison in 1914, 5 developed the disease in from four to eighteen days after having been detected as carriers. In order to detect carriers who might otherwise escape in the routine examination at the cholera hospital in Manila, a follow-up system has been adopted. Cholera carriers and cases are discharged from the hospital after 3 successive negative examinations of the fæces at 2-day intervals. All cholera carriers and recovered cholera cases are followed to their homes and examined weekly for a period of two months. If they are found positive, they are returned to the hospital. About 27 cases were so returned in eight weeks.

The development of antibodies against the cholera vibrio in cases of cholera appears to be rather inconstant. Agglutinins for the cholera vibrio have been found in the blood of cholera patients by Achard and Bensaude,(1) Haller,(23) Karwacki,(26) Schirnow,(41) Kopp,(28) Svenson,(43) Oya,(35) Greig,(17) and many others. Even when agglutinins are present, they are not in great abundance, as the titer of the serum is in the majority of the cases below 1:500. Kolle and others have shown that normal sera may agglutinate the cholera vibrio in dilutions up to 1:20. At any rate, the reaction is of limited diagnostic importance in cases of cholera, for it is usually absent in fatal cases, and the agglutinins do not appear to any extent in the blood until convalescence has commenced.(17) Greig thinks that the reaction may be of value in the prognosis of cholera cases, in as much as he found that agglutinins appeared earlier and in greater amounts in nonfatal cases. He also thinks that the reaction may be a valuable preliminary test in the detection of convalescent cholera-carrier cases.

Another point of undetermined importance in dealing with the cholera epidemics is the significance to be attached to the finding of choleralike vibrios in the stools or tissues of persons under examination. Opinions on this question are not as yet unanimous for lack of positive evidence. These vibrios may have all the characters of the true cholera vibrios save that they are not agglutinated by high-titer cholera-agglutinating serum and do not, when injected intravenously into rabbits, produce

a serum that agglutinates the true cholera vibrio. They are strongly hæmolytic and liquefy gelatin faster than do the true cholera vibrios. Such nonagglutinable choleralike vibrios have been found in cases that have no relation to cholera and in true cholera cases either in association with the true cholera vibrio or after the true cholera vibrio has disappeared. Evidence varies as to whether it is possible for the true cholera vibrio to lose its agglutinability; it seems probable that the agglutinogenic capacity of the true cholera vibrio is more constant than its agglutinability.

O'Connell(33) states:

> These choleroid organisms are an extremely interesting phenomenon. Their relationship to true cholera may be said to have been established but not defined. Bacteriologists in service in the Far East have noted their appearance in specimens subjected to microscopical examination immediately before and during cholera epidemics. They are not known where cholera is not or has not been recently. Their morphology and biological characteristics are such that it is impossible to distinguish them from true cholera organisms by microscopic examination. Agglutination is the only test under which their reaction is differentiated from that of the cholera vibrio.

Certain authors, Zlatogoroff(45) and Horowitz,(24) have made the assertion that under certain conditions of growth and environment the cholera organism loses all or some of its typical biological characters, regaining them under certain favorable circumstances. Clinicians in the Philippines have repeatedly made the statement that cholera was endemic, notably Heiser(21) and Clements,(4) although the diagnosis was unconfirmed bacteriologically. Any purely theoretical conjecture such as this, unsupported by exact laboratory evidence, must be set aside, and the final decision must be based on experimental facts with absolute exclusion of possible error. The causal relation between the seasonal outbreaks of cholera in India and the vitality of the cholera vibrio outside the human body has already been demonstrated by Greig.

Few of the known microörganisms in the etiology of human diseases appear to be so variable in their morphology as the cholera vibrio. Ohno(34) has called attention to the striking changes noted in shape and motility in cholera strains, and Hovorka(25) has mentioned the impairment of agglutinability. Such changes as these do not seem to be permanent, and some of the causative factors are known, so that it is possible practically to cause such changes to appear at will.

It has been well established that the reported inagglutinability of certain cholera strains was due to the use of an immune

serum of low potency; also certain strains were found to agglutinate with immune rabbit serum, but not with immune horse serum. Zlatogoroff(45) was able to produce agglutination in an imperfectly agglutinable strain of cholera by repeated passage through animals. On the other hand, McLaughlin and Whitmore(31) were unable to confirm Zlatogoroff's work.

Our own work, based on the study of cases of cholera and cholera carriers after death, will now be presented.

From July, 1915, until the present time the intestinal contents and gall bladder from all autopsies have been examined for cholera vibrios as a routine procedure.

Technic.—A loop of small intestine about 0.5 meter from the cæcum was ligatured, severed from its connections, placed in a new, clean, self-sealing jar, and transported to the laboratory for bacteriological examination. In the same way the bile ducts were ligatured and severed, and the gall bladder was removed without opening, placed in another new, clean jar, and transported to the laboratory. The specimen as received at the laboratory was handled with sterile instruments. The outer surface of the intestine was seared with a hot spatula, and with a sterile scalpel an incision was made into the lumen of the gut. If the contents were fluid, 1 cubic centimeter was removed with a sterile pipette and inoculated into a cholera peptone tube. The last drop in the pipette was allowed to fall on a Dieudonné plate and was then spread with a sterile platinum loop. If the fæces were solid, 1 standard loop (4 millimeters) was inoculated into peptone and also smeared on a Dieudonné plate. The same procedure was followed with the gall bladder. These direct plates and peptone tubes were incubated overnight at 37.5° C. In the event of the plate remaining sterile the next morning, the peptone tubes were examined that morning for organisms of suspicious motility and new Dieudonné plates were seeded from those plates with suspicious organisms. Suspicious colonies on Dieudonné plates were picked, emulsified in physiologic salt solution, and tested for agglutination with a cholera-immune goat serum of titer 1: 6000, in dilution of 1: 500.

There have been 269 cases in which there has been reason clinically, anatomically, or bacteriologically to suspect the presence of Asiatic cholera. In 22 of these, vibrios were not found, and 5 cases were known to have been carriers of the vibrios at varying periods before death. These latter 27 cases will be discussed later. Of the remaining 242 cases, 32 were interpreted as cholera carriers and 210 as true cholera cases.

The classification of all of these cases is presented in Table II.

TABLE II.—*Classification of cases under consideration.*

		I.	II.	III.	IV.
		Intestine+, Bile+	Intestine+, Bile—	Intestine—, Bile+	Intestine—, Bile—
a	Clinically positive; anatomically positive	Cholera, 72	Cholera, 42	Cholera, 5	Cholera, 2.
b	Clinically suspicious; anatomically positive	Cholera, 25	Cholera, 13	Cholera, 1	Cholera, 2.
c	Clinically positive; anatomically suspicious	Cholera, 9	Cholera, 5	Cholera, 1	Cholera, 2; clinical error, 1.
d	Clinically positive; anatomically negative	Cholera, anatomic error, 1	Cholera, anatomic error?, 1	0	Not cholera, clinical errors, 4.
e	Clinically suspicious; anatomically suspicious	Cholera, 4	Cholera, 1	0	Possibly not cholera, 2.
f	Clinically suspicious; anatomically negative	Cholera, anatomic errors, 2	0	Carriers, 2	Not cholera, 8.
g	Clinically negative; anatomically positive	Cholera, clinical error, 1	0	0	0
h	Clinically negative; anatomically suspicious	Cholera, clinical errors, 4	Cholera, clinical errors, 2	0	Probably not cholera, 1.
i	Clinically negative; anatomically enteritis	0	Cholera, clinical error, 1	Cholera, clinical error, 1	0
j	Clinically negative; anatomically negative	Carriers, 10; cholera, 4	Carriers, 5; cholera case, 1	Carriers, 11; cholera case, 1	0
k	Clinically undetermined; anatomically positive	Cholera, 1	0	0	0
l	Clinically undetermined; anatomically enteritis	0	Carrier (poison), 1	Cholera, 1	0
m	Clinically undetermined; anatomically negative	Cholera, anatomic errors, 2	0	Carrier, 1	0
n	Clinically enteritis; anatomically enteritis	0	Cholera, 5	Cholera, 2	0
o	Clinically enteritis; anatomically negative	0	Cholera, anatomic error, 1; carriers, 2.	0	0
p	Known carriers	0	0	Carrier, 1	4

Note:—"Clinically positive" means in the majority of cases that the vibrios were isolated from the fæces before death.

"Clinically suspicious" means that there were symptoms pointing to cholera, but bacteriologic examination had not been made before death.

"Anatomically positive" means that at autopsy the case was declared cholera by the pathologist on anatomic grounds.

"Anatomically suspicious" means that at autopsy the case was declared "possibly cholera" or "probably cholera" by the pathologist when the anatomic picture was obscure, as so often happens in children, in decomposed bodies, and in adults in whom cholera has been superimposed on other extensive disease. [See Crowell, Notes on the diagnosis of Asiatic cholera at autopsy, *This Journal, Sec. B* (1914), **9**, 361.]

The cases classified as clinically or anatomically "enteritis" were so diagnosed either during life or at autopsy without reference being made to their possible origin.

"Clinical error" means that the case either was diagnosed clinically as cholera when it proved not to be so, or was not diagnosed cholera when it did prove to be so. Many of these cases were not in hospital, but were sent direct to the morgue for diagnosis from their homes, where they were often seen by a physician only after death.

"Anatomic error" means that the case was undetected as cholera at autopsy. In the majority of cases this was accounted for by the presence of other extensive intestinal diseases, the chief of which was tuberculosis.

148932—4

CHOLERA CASES

In the 210 cases of cholera, the cholera vibrio was isolated from both the intestinal contents and the gall bladder in 59.5 per cent (125 cases), from the intestine alone in 34.2 per cent (72 cases), and from the gall bladder alone in 5.7 per cent (12 cases). Combining these figures, we see that the cholera vibrio was isolated from the intestine in 93.7 per cent of the cholera cases and from the gall bladder in 65.2 per cent of the cholera cases.

These figures emphasize the importance of the bacteriologic examination of both the intestine and the gall bladder in cases suspected of harboring the cholera vibrio. The number of cases that would have been declared bacteriologically not cholera following examination of the intestine alone is 5.7 per cent. It is also seen that, in cholera cases, examination of the intestine alone is better than examination of the gall bladder alone by 28.5 per cent.

These facts are summarized in Table III.

TABLE III.—*Bacteriologic examination of 210 cases of Asiatic cholera.*

	Per cent.
Intestine+, bile+	59.5
Intestine+, bile−	34.2
Intestine−, bile+	5.7
Intestine+	93.7
Bile+	65.2

CHOLERA CARRIERS DETECTED POST MORTEM

Among the 269 cases of which this paper treats, there were detected 32 cases which were diagnosed as cholera carriers after full consideration of all available clinical, anatomic, and bacteriologic data. In none of these cases was there anything clinically or anatomically to indicate that they might have been cholera cases, with one exception. The exception was a poisoning case with an enterocolitis, which aroused the suspicion of cholera in the mind of the pathologist before the history was known.

It is not possible for us to trace possible associations between these carrier cases and known cholera cases.

Considering these 32 cases bacteriologically we find that cholera vibrios were found in both the intestine and gall bladder in 31.2 per cent (10 cases), only in the intestine in 25 per cent (8 cases), and only in the gall bladder in 43.7 per cent (14

cases). Combining these figures it is seen that in 56.2 per cent of the carrier cases vibrios were isolated from the intestine and in 75 per cent from the gall bladder. From these figures we see that in carrier cases, in contrast to what has been shown above in true cholera cases, the vibrios were found in the gall bladder 18.8 per cent more frequently than in the intestine.

These facts are summarized in Table IV.

TABLE IV.—*Bacteriologic examination of 32 cholera-carrier cases detected post mortem.*

	Per cent.
Intestine+, bile+	31.2
Intestine+, bile−	25
Intestine−, bile+	43.7
Intestine+	56.2
Bile+	75

These carrier cases are considered to be of such importance that the main facts concerning them are set forth in Table V.

CASES KNOWN TO HAVE BEEN CHOLERA CARRIERS

Five cases which were known to have been cholera carriers have been autopsied. Cholera vibrios had been isolated from the fæces of these cases at periods of thirty-seven to one hundred seventeen days before death. Between the time of isolation of the vibrios and death, from 12 to 24 successive negative examinations for the vibrios had been made.

Careful search was made in these cases for some possible hidden focus of cholera infection, and numerous cultures from various parts of the body were made. In 4 of these 5 cases no vibrios were found after death. In the fifth case, which had been positive thirty-seven days before death and had since had 12 successive negative examinations, a cholera vibrio was isolated from the bile and a nonagglutinable vibrio from the jejunum and upper and lower ileum. Liver, spleen, cæcum, and sigmoid showed no vibrios in smears or cultures. This case died of pneumonia and a paratyphoid infection. It is to be noted that the interval between the detection of this case as a carrier and his death was the shortest of any of these cases that were examined. Therefore this is the case in which there was the greatest possibility of finding the organism. The data concerning these cases are presented in Table VI.

TABLE V.—*Cholera-carrier cases detected post mortem.*[a]

Autopsy No.	Clinical diagnosis.	Duration of illness.	Anatomic diagnosis.	Bacteriologic examination of—		Age.
				Intestine.	Bile.	
4907	Meningeal tuberculosis	2 weeks	General miliary tuberculosis	+	+	5 months.
5029	do	14 days	Fracture of skull	+	+	28 years.
4961	Pulmonary tuberculosis	37 days	Pulmonary tuberculosis	+	+	23 years.
5022	do	6 months	do	+	+	50 years.
5345	do	2 months	do	+	+	5 years.
5016	do	3 days	Lymphosarcoma of intestine	+	+	40 years.
5303	Typhoid	11 days	Pneumonia	+	+	19 years.
5017	Broncho-pneumonia	5 days	Bacillary dysentery	+	+	2 years.
5163	Lobar pneumonia	16 days	Lobar pneumonia	+	+	6.5 months.
5353	Burn	4.5 hours	Burn	+	+	9 months.
5010	Abscess of liver	20 days	Abscess of liver	+	−	45 years.
5054	Septicæmia	4 days	Ruptured abdominal aneurism	+	−	36 years.
5215	Meningitis	17 days	Meningitis	+	−	21 years.
5309	Chronic nephritis	2 months	Chronic nephritis	+	−	69 years.
5360	Tuberculosis	1.5 years	Tuberculosis	+	−	18 years.
5012	Undetermined	(?)	Enterocolitis (poisoning)	+	−	33 years.
5110	Chronic enteritis	2 months	Decomposition	+	−	23 years.
5310	Enteritis	(?)	Tuberculosis	+	−	(?)
5314	Undetermined	(?)	Submersion	−	+	36 years.
5211	Pneumonia (known carrier)	1.5 months	Pneumonia	Choleralike vibrio.	+	26 years.
4840	Pulmonary tuberculosis	(?)	Tuberculous enteritis	−	+	22 years.
4849	do	1 year	Malaria	−	+	23 years.
4906	Meningeal tuberculosis	15 days	General miliary tuberculosis	−	+	1 year.
4997	Pulmonary tuberculosis	1 year	Pulmonary tuberculosis	−	+	19 years.
5165	do	1 year	do	−	+	22 years.
5177	do	1 year	do	−	+	30 years.

5244	do	2 months	do	—	+	21 years.
5164	do	36 days	Lobar pneumonia	—	+	65 years.
5001	Typhoid	23 days	Malaria	—	+	23 years.
5338	Accident	5 hours	Accident	—	+	12 years.
5442	Malaria	10 days	Malaria	—	+	50 years.
4942	Undetermined	3 days	Cirrhosis of liver	—	+	36 years.
5070	do	(?)	Cellulitis	—	+	24 years.

[a] See note to Table II.

TABLE VI.—*Data concerning known carrier cases.*

Autopsy No.	Clinical diagnosis.	Anatomic diagnosis.	Age.	Duration of illness.	Interval between detection and death.	Number successive negative examinations.	Bacteriologic examination after death.
					Days.		
5367	Tuberculosis	Tuberculosis	23	8 months	111	24	Gall bladder, intestine, spleen, blood, and pericardial fluid negative.
5368	Amœbiasis	Bacillary colitis	22	9 days	117	17	Gall bladder, jejunum, duodenum, ileum, colon, and liver negative.
5372	Tuberculosis	Tuberculosis	24	2.5 months	96	21	Spleen, gall bladder, blood, duodenum, jejunum, upper ileum, lower ileum, ascending colon, sigmoid, and appendix negative.
5413	do	do	47	5 months	111	12	Gall bladder and intestine negative.
5211	Pneumonia	Pneumonia and typhoid.	26	1.5 months	87	12	Bile positive. From jejunum and upper and lower ileum a nonagglutinable vibrio was isolated. Liver, spleen, cæcum, and sigmoid negative.

NONAGGLUTINABLE VIBRIOS

Vibrios which were not agglutinable by a standard cholera-immune serum were found in 6 cases. It is very probable that they would have been found in more cases, but special search for them was made only during the latter part of the investigation. The data concerning these cases is presented in Table VII.

TABLE VII.—*Data concerning cases from which nonagglutinable vibrios were isolated.*

Autopsy No.	Clinical diagnosis.	Anatomic diagnosis.	Bacteriologic examination of—	
			Intestine.	Bile.
4827	Undetermined	Acute cardiac dilatation.	Nonagglutinable vibrio.	Cholera vibrio.
5211	Pneumonia (known carrier).	Pneumonia	do	Do.
5315	Cholera	Probable cholera	do	Negative.
5397	Cardiac disease	Tuberculosis	do	Nonagglutinable vibrio.
5410	Tuberculosis	do	do	Negative.
5429	Accident	Pneumonia	do	Do.

Since early in 1915 some 30 strains of nonagglutinable vibrios isolated from the fæces and gall bladder of positively known cholera patients and from the fæces of cholera contacts and other persons have been studied definitely to prove, if possible, the true status of the strains—that is, whether or not they were to be regarded as of significance, and if they should prove to be of significance, whether the carriers of the nonagglutinable vibrios should be regarded as a menace to public health.

Method.—Specimens were taken by means of sterile cotton swabs on pieces of bamboo. As taken, these were placed in sterile tubes containing about 2 cubic centimeters of 3 per cent agar of −1 reaction to phenolphthalein. When received at the laboratory, 10 cubic centimeters of a double-strength peptone were added, and the tubes were incubated overnight, or about eighteen hours, at 37.5° C. Hanging drops were then made and examined for suspicious motility. Dieudonné plates were seeded from all suspicious tubes, and suspicious colonies were fished at the end of a further 24 hours' incubation; the agglutinability was tested with a dilution of 1: 500 of cholera-immune goat serum, titer 1: 6,000. All of these strains of organisms were tested for their agglutinability, but none gave any reaction. They were then transplanted to pure beef bile with transfers to agar every

three days, and the agglutinability was tested each time. After forty transfers, 8 (6 from fæces of cholera carriers and 2 from cholera cases) of these strains showed prompt agglutination in dilution of 1 : 500 of an immune serum by the microscopic method and up to 1:4,000 by the macroscopic method.

Of these strains but 5 held this apparently acquired property of agglutination for any length of time, the other 3 losing it after cultivation for a period of two months. The strains which now agglutinate do not agglutinate as promptly as they did when the property was first acquired about three months ago, but it is still sufficiently quick to warrant their being classed as true cholera organisms on the basis of agglutination.

The 30 strains studied resembled the true cholera vibrio morphologically; all were monociliate and actively motile. All produced indol in peptone water and typical liquefaction in gelatin and growth on Dieudonné. They differed in that, with the exception of the 8 strains noted, none were agglutinated by a high-titer cholera serum. When injected into guinea pigs they did not produce agglutinin which agglutinated a standard cholera vibrio, except that 2 of the 5 strains, which acquired the agglutinating property, did after this acquisition produce a serum which partially agglutinated a standard vibrio in dilution up to 1:100.

CASES IN WHICH CHOLERA VIBRIOS WERE NOT FOUND

Twenty-two cases in which cholera vibrios were not found are included in this study on account of their clinical or anatomic features. In 6 of these it is considered that the patients had cholera in spite of the fact that no vibrios were found in either the intestine or gall bladder. This conclusion is based on the clinical and anatomic features shown in Table VIII. Thirteen cases in which there was some reason either clinically or anatomically to suspect cholera were considered not to be cholera after all data were available. Three cases which were clinically and anatomically suggestive of being cholera were considered, in the light of all the evidence, as probably not cholera, but a definite diagnosis on them is reserved. Greig,(20) in a very recent article, states that in 72 out of 659 cholera cases examined no vibrio was found. He also includes as cholera cases 51 other cases in which only a choleralike vibrio was found. It may be noted that in only 6 of the 221 cases considered cholera did we fail to find the true cholera vibrio. Thirteen cases in our series, which were suspected either clinically or anatomically of being cholera, were eliminated from the list of cholera cases after careful consid-

TABLE VIII.—*Data concerning cases in which no vibrios were found.*[a]

Group.	Autopsy No.	Clinical diagnosis.	Anatomic diagnosis.	Age.	Duration of illness.	Hours post mortem.	Conclusion.
IVa	4934	Cholera	Cholera	71 years	9 hours	13	Probably cholera.
	4936	do	do	3 years	3 days	18	Do.
IVb	5092	Suspect cholera	do	6 years 9 months	10 days	35	Do.
	5132	do	do	3 years 7 months	7 days	7	Do.
IVc	5114	Cholera	Possible cholera	30 years	6 days	40	Probably not cholera; extensive decomposition.
	5325	do	Probable cholera	17 years	3 days	26	Looks like cholera.
	5337	do	do	37 years	4 days	12	Do.
IVd	5002	do	Mitral endocarditis	45 years	(?)	----------	Not cholera.
	5323	do	Cirrhosis of liver	55 years	5 hours	24	Do.
	5463	do	Tuberculosis	30 years	(?)	11	Do.
IVe	5237	Suspect cholera	Probable cholera	5 years	14 days	17	Probably not cholera.
	5276	do	Possible cholera	1 year	3 days	14	Do.
	5069	do	Amœbic colitis	2 years 5 months	5 months	18	Not cholera.
	5095	do	Bacillary colitis	7 years	(?)	12	Probably not cholera.
	5241	do	Acute cardiac dilatation	22 years	16 hours	8	Pure heart case.
	5250	do	Pulmonary tuberculosis	25 years	do	4	Tuberculous case with heart failure.
IVf	5320	do	Pneumonia	80 years	7 days	15	Not cholera.
	5354	do	Strangulated mesenteric hernia.	23 years	1 day	7	Do.
	5362	do	Typhoid	30 years	(?)	43	Do.
	5321	do	Tuberculosis	20 years	2 days	6	Do.
IVh	5394	Infantile beriberi	Probable cholera	4 months	7 days	13	Probably not cholera.

[a] See note to Table II.

eration of all the circumstances. If we have made an error in this, it has been on the conservative side.

Some of the details concerning this group of cases are presented in Table VIII.

The general data concerning all the cases under investigation follow:

TABLE IX.—*Group I. Cases in which the cholera vibrio was isolated from the intestine and the bile.* [a]

Group.	Autopsy No.	Number of cases.	Clinical diagnosis.	Anatomic diagnosis.	Remarks.
Ia		72	Cholera	Cholera	
Ib		25	Suspected cholera	do	
Ic		9	Cholera	Suspected cholera	
Id	5336	1	do	Tuberculosis	Cholera obscured by tuberculosis at autopsy.
Ie		4	Suspected cholera	Suspected cholera	
If	5159	2	do	Tuberculosis	Cholera obscured by tuberculosis at autopsy.
	5206		do	Hypernephroma	Cholera obscured by tumor at autopsy.
Ig	5299	1	Tuberculosis	Cholera	Clinically undetected.
Ih	5121	4	Chronic enteritis	Probable cholera	Clinically undetected. 4 years old.
	5133		Tuberculosis	Acute enteritis	Clinically undetected. 3½ years old.
	5356		Infantile beriberi	Slight enteritis	Clinically undetected. 4 years old.
	5359		Typhoid	Possible cholera	Clinically undetected. 7 years old.
Ij	4907	14	Meningeal tuberculosis.	General miliary tuberculosis.	Carrier case.
	5029		do	Fracture skull	Do.
	5176		do	Intestinal tuberculosis.	May be a cholera case; 2½ years old; 18 hours' illness.
	4961		Pulmonary tuberculosis.	Pulmonary tuberculosis.	Carrier case.
	5022		do	do	Do.
	5345		do	do	Do.
	5016		do	Sarcoma, intestinal	Do.
	5039		Typhoid	Typhoid	Probably a cholera case. 5 years old.
	5303		do	Pneumonia	Carrier case.
	4947		Acute cardiac dilatation.	Acute cardiac dilatation.	Cholera case; obscured by bismuth at autopsy.
	5018		Chronic ileocolitis	Dilated heart, anæmia, etc.	Probably a cholera case; 3½ years old.
	5017		Bronchopneumonia	Bacillary colitis	Probable carrier.
	5163		Lobar pneumonia	Lobar pneumonia	Carrier.
	5353		Burns	Burns	Do.
Ik	5008	1	Undetermined	Cholera	
Im	4827	2	do	Cardiac dilatation	Cholera case, anatomically undetected.
	5358		do	Tuberculosis	Do.

[a] See note to Table II.

TABLE X.—*Group II. Cases in which cholera vibrio was present in the intestine but not in the bile.*[a]

Group.	Autopsy No.	Number of cases.	Clinical diagnosis.	Anatomic diagnosis.	Remarks.
IIa		42	Cholera	Cholera	Cholera case.
IIb		13	Suspected cholera	do	Do.
IIc	4871	5	Cholera	Possible cholera	Do.
	4959		do	(?)	Do.
	5090		do	Acute catarrhal enteritis.	Do.
	5091		do	do	Do.
	5315		do	Probable cholera	Do.
IId	5161	1	do	Typhoid	Anatomically undetected.
IIe	4992	1	Suspected cholera	Probable cholera	Cholera case.
IIh	4881	2	Ascariasis	do	Infant; clinically undetected.
	5009		Mumps	do	Do.
IIi	4828	1	Marasmus	Catarrhal enteritis	Do.
IIj	5010	6	Abscess of liver	Abscess liver	Carrier case.
	5054		Septicæmia	Ruptured abdominal aneurism.	Do.
	5215		Meningitis	Meningitis	Do.
	5309		Chronic nephritis	Chronic nephritis	Do.
	5329		Beriberi	Beriberi ?	Probably a cholera case; 3 months old; 3 days illness.
	5360		Tuberculosis	Tuberculosis	Carrier.
III	5012	1	Undetermined	Acute hemorrhagic enterocolitis.	Carrier—poisoning case.
IIn	4889	5	Acute ileocolitis	Probable cholera	Cholera case; infant.
	5007		Acute enterocolitis	do	Do.
	5030		do	Acute enterocolitis	Do.
	5052		Gastroenteritis	Acute enteritis	Do.
	4971		Cholera infantum	Acute enterocolitis	Do.
IIo	4932	3	Acute ileocolitis	Pulmonary tuberculosis.	Probably cholera case.
	5110		Chronic enteritis	Decomposition	Probably carrier.
	5310		Enteritis	Tuberculosis	Carrier.

[a] See notes to Table II.

TABLE XI.—*Group III. Cases in which cholera vibrio was present in the bile but not in the intestine.*[a]

Group.	Autopsy No.	No. of cases.	Clinical diagnosis.	Anatomic diagnosis.	Remarks.
IIIa		5	Cholera	Cholera	Cholera cases.
IIIb	4987	1	Suspected cholera	do	Do.
IIIc	4866	1	Cholera	Possible cholera	Do.
IIIf	4942	2	Suspected cholera	Cirrhosis of liver	Carrier.
	5070		do	Suppurative cellulitis.	Do.
IIIi	5160	1	Meningeal tuberculosis.	Acute catarrhal enteritis.	Probable cholera case; infant.
IIIj	4840	12	Pulmonary tuberculosis.	Tuberculous enteritis.	Carrier case.
	4849		do	Malaria	Do.
	4851		do	Pulmonary tuberculosis.	May be cholera case.
	4906		Meningeal tuberculosis	General miliary tuberculosis.	Carrier case.
	4997		Pulmonary tuberculosis.	Pulmonary tuberculosis.	Do.
	5165		do	do	Do.
	5177		do	do	Do.
	5244		do	do	Do.
	5164		do	Lobar pneumonia	Do.
	5001		Typhoid	Malaria	Do.
	5338		Accident	Accident	Do.
	5422		Malaria	Malaria	Do.
IIIl	5295	1	Undetermined	Possible cholera	Cholera case.
IIIm	5314	1	do	Submersion	Do.
IIIn	4836	2	Acute ileocolitis	Probable cholera	Cholera case; infant.
	5147		do	do	Do.
IIIp	5211	1	Known carrier (pneumonia).	Pneumonia	Carrier case.

[a] See note to Table II.

SYNOPSIS

The intestinal contents and the bile of 269 cases of cholera and cholera carriers have been examined. In 212 cases of cholera the vibrio was found in the bile in 65.2 per cent and only in the bile in 5.7 per cent. In 32 cholera carriers detected after death, the cholera vibrio was found in the bile in 75 per cent and only in the bile in 43.7 per cent.

In examining a large series of cholera cases the vibrio may not be recovered from the fæces in a certain number in which it is recovered from the bile. In cholera carriers the vibrio was present in this series in the bile in 10 per cent more cases than in cholera cases and only in the bile in 38 per cent more than in cholera cases. From this the importance of routine examination of both bile and fæces becomes apparent.

Five cases that were known to have been carriers before death were examined after death, and only in the one with the shortest period between detection and death (thirty-seven days) was the vibrio found. In that case the vibrio was isolated from the bile only.

Thirty strains of nonagglutinable vibrios, isolated from the fæces and bile of cholera cases, cholera contacts, and others, have been studied. When first isolated, these were not agglutinated by high-titer cholera-immune serum. By growth in bile 8 of these strains acquired the agglutinability. Five of these 8 strains retained this property, and the other 3 lost it after cultivation for a period of two months.

In 6 cases that were clinically and anatomically cholera, the cholera vibrio was not isolated from either the fæces or the bile. Such cases occur in a large series of cholera cases.

REFERENCES

1. Achard and Bensaude. *La Semaine med.* (1897), 151.
2. Amako. *Centralbl. f. Bakt., Orig.* (1908), **48**, 602.
3. Bruloff. *Russkyi Vratch* (1910), No. 47, 1821.
4. Clements. *Phil. Journ. Sci., Sec. B* (1908), **3**, 185.
5. Defressine and Cazeneuve. *Compt. rend. Soc. biol.* (1912), **72**, 933–935.
6. Doyen. *Arch. Physiol. norm. et pathol.* (1885) (III), **6**, 179.
7. Flu. *Geneesk. Tijdschr. Nederl. Indië* (1914), **54**, 524.
8. Girode. *Compt. rend. Soc. biol.* (1893) (III), **9**, 507.
9. Greig. *Ind. Journ. Med. Research* (1913), **1**, 44.
10. Idem. Ibid. (1913), **1**, 59.
11. Idem. Ibid. (1913), **1**, 65.
12. Idem. Ibid. (1913), **1**, 90.
13. Idem. Ibid. (1913), **1**, 290.
14. Idem. Ibid. (1914), **2**, 1.
15. Idem. Ibid. (1914), **2**, 28.

16. IDEM. Ibid. (1914), **2**, 608.
17. IDEM. Ibid. (1914), **2**, 733.
18. IDEM. Ibid. (1915–16), **3**, 442.
19. IDEM. Ibid. (1915–16), **3**, 628.
20. IDEM. Ibid. (1917), **4**, 651.
21. HEISER. *Phil. Journ. Sci., Sec. B* (1908), **3**, 89.
22. International Sanitary Conference at Paris (1911).
23. HALLER. *Russkyi Vratch* (1905), 689.
24. HOROWITZ. *Centralbl. f. Bakt., Orig.* (1911), **58**, 79.
25. HOVORKA J., and HOFER, B. Ibid. (1913), **71**, 103.
26. KARWACKI. *Zeitschr. f. Hyg. u. Infektionskrankh.* (1906), **54**, 39.
27. KELSCH and VAILLARD. *Arch. physiol. norm. et pathol.* (1885) (III), **5**, 341–384.
28. KOPP. *Russkyi Vratch* (1909), 185.
29. KULESCHA. *Klin. Jahrb.* (1910), **24**, 137.
30. KÜSTER and GÜNZLER. *Zeitschr. f. Hyg. u. Infektionskrankh.* (1916), **81**, 447.
31. MCLAUGHLIN and WHITMORE. *Phil. Journ. Sci., Sec. B* (1910), **5**, 403.
32. NICATI and RIETSCH. Recherches sur la cholera. F. Alcan, Paris (1886).
33. O'CONNELL. *Annual Rep. Health Officer, Port of New York* (1915), 14.
34. OHNO. *Phil. Journ. Sci., Sec. B* (1908), **3**, 341.
35. OYA. *Centralbl. f. Bakt., Ref.* (1903–1904), **34**, 202.
36. PFEIFFER and KOLLE. *Centralbl. f. Bakt., 1.* Abt. (1896), **20**, 129.
37. PIROGOFF. Die pathologische Anatomie der Cholera u.s.w. St. Petersburg (1850). (Cited by Kulescha, No. 29.)
38. RAPCHEVSKI. *Vrach* (1886), No. 4, 5.
39. REKOWSKI and DZIERZGOWSKI. *Arch. sci. biol.*, St. Petersburg (1892), **1**, 167.
40. SAWTSCHENKO, I. G. *Vrach* (1893), No. 21.
41. SCHIRNOW. *Russkyi Vratch* (1908), No. 8.
42. SCHÖBL. *Phil. Journ. Sci., Sec. B* (1915), **10**, 11.
43. SVENSON. *Zeitschr. f. Hyg. u. Infektionskrankh.* (1909), **64**, 342.
44. TIZZONI and CATTANI. *Ziegler's Beitr.* (1888), **3**.
45. ZLATOGOROFF, S. J. *Centralbl. f. Bakt., Orig.* (1911), **58**, 14.

Issued with THE PHILIPPINE JOURNAL OF SCIENCE, SECTION B,
Tropical Medicine, Vol. XII, No. 2, March, 1917.

PROCEEDINGS OF THE MANILA MEDICAL SOCIETY

REGULAR MONTHLY MEETING, FEBRUARY 13, 1917

The business brought before the society is presented in the secretary's minutes, which follow:

The regular monthly meeting of the Manila Medical Society was held at 8.30 in the evening, February 13, 1917, in the College of Medicine and Surgery, Manila, with Lieut. Col. Winter in the chair and with 36 members and 6 visitors present.

The minutes of the last meeting were read and approved as read.

The secretary read a communication from the Daughters of the American Revolution inviting the members of the society to hear Mrs. Winterhalter's paper on the Navy League, to be given at the Columbia Club Hall on February 19, 1917.

The council recommended the following names for election as active members of the society: Lieut. Col. F. A. Winter, M. C., U. S. Army; Capt. J. M. Willis, M. C., U. S. Army; Dr. Ricardo Fernandez y Asis; and Dr. Harry H. Steinmetz. It was moved, seconded, and carried that the society ratify the recommendation of the council.

The resignation of Prof. F. G. Haughwout as editor of the proceedings of the Manila Medical Society, its acceptance by the president, and the approval by the council were presented to the society. It was moved, seconded, and carried that the resignation of Professor Haughwout as accepted by the president and approved by the council be ratified by the society.

It was moved, seconded, and carried that the resignation of Lieut. Col. S. C. Gurney as a member of the council, because of his departure for the United States, be accepted.

The president appointed the following nominating committee to select the candidates to fill the vacancies in the council made by the expired term of Dr. N. M. Saleeby and the resignation of Lieut. Col. S. C. Gurney:

Dr. Otto Schöbl. Dr. E. S. Ruth. Capt. John H. Trinder.

The appointment of Dr. R. B. Gibson by the council as editor of the proceedings of the Manila Medical Society was presented for ratification and approved by the society.

The report of the program committee of the Corregidor meeting on January 6, 1917, was referred by the president to the secretary. The report is as follows:

REPORT OF PROGRAM COMMITTEE APPOINTED BY THE PRESIDENT, DECEMBER 9, 1916

On December 10 the program committee, appointed by Dr. B. C. Crowell, met at the College of Medicine and Surgery and accepted the kind invitation of the medical officers stationed at Fort Mills to hold the combined annual and regular monthly meeting of the Manila Medical Society in the recreation room of the post hospital at Corregidor on the evening of January 6, 1917.

Through the concerted action of the various heads of the military service, both at Manila and Corregidor, very obliging arrangements were perfected in which the Quartermaster Corps scheduled the U. S. Army transport *Merritt* for transportation on this occasion.

The distance to Corregidor is approximately 40 kilometers, and it takes about two and one-half hours to make the trip. The program arranged for this time is set forth in General Orders No. 99, Headquarters Manila Medical Society, U. S. Army Transport *Merritt*, dated January 6, 1917, a copy of which is attached hereto.

The courtesies shown upon the arrival at Corregidor readily revealed that every detail had been considered by the hosts in preparing for the event. Special cars were kindly furnished by the Quartermaster Corps, and the crowd was taken to the beautiful, modern, concrete hospital building, the recreation room of which had been so carefully and completely decorated and prepared as to give the feeling of cordial welcome the moment one entered.

The program as indicated in the minutes ended about 11.30 and as many as could make it possible remained at Corregidor for the night, while the rest returned to Manila about 3 o'clock on the morning of the 7th.

H. G. MAUL, *Chairman*,
D. DE LA PAZ,
J. E. REED, Jr.,
Program Committee.

The report of the committee on the revision and bringing up to date of the constitution and by-laws of the society, composed of Drs. J. A. Johnston, C. H. Manlove, and R. B. Gibson, was presented and approved as revised by the committee.

The president referred to the secretary the report of the committee on the program for the next three months. The report is as follows:

PROGRAM FOR FEBRUARY, 1917, MEETING

1. The program committee presents the following:

The regular monthly meeting of the Manila Medical Society will be held in the College of Medicine and Surgery, on Monday evening, February 12, at 8.30 in the evening. The topic for discussion will be: Recent advances in the diagnosis and treatment of anterior poliomyelitis. The program will include:

Address. Lieut. Col. Francis A. Winter.
Clinical aspects of anterior poliomyelitis. Maj. Henry H. Rutherford.

The problem from the standpoint of the Public Health Service. Dr. Hugh de Valin.

The bacteriology and serology of anterior poliomyelitis. Dr. John A. Johnston.

Discussions by Drs. N. M. Saleeby, William E. Musgrave, and J. E. Reed, jr.

2. It is requested that in order not to bring this subject before the public, this program be withheld from the newspapers.

C. C. HILLMAN,
Captain, Medical Corps, U. S. Army,
Chairman.

The nominating committee for the election of two councilors reported the names of Dr. N. M. Saleeby for five years and Dr. B. C. Crowell for two years, and their election was voted favorably by the society.

The program for the evening was then carried out.

H. G. MAUL,
Secretary-Treasurer,
Manila Medical Society.

SCIENTIFIC PROGRAM

PRESIDENT'S ADDRESS

By Lieut. Col. F. A. WINTER

I do not believe that I could better use the brief measure of your time, which is given me, than by taking the opportunity to say a word to you on the subject of Manila as it appears to-day to one who saw it first in 1899, just after the American occupation. The contrast picture is full of interest and instruction.

It was very rightly stated in those days that Manila was a startling demonstration of civic capabilities in the matter of dirt and stinks. It needed but the casual attention of any seeker to get confirmation of this, and a teeming population struggling for existence in a sea of mud, during the rains, with the most meager provision of sanitary systems, fully completes the description.

To one coming here eighteen years later, the evidence of civic betterment is so striking that it brings surprise—I might almost say, unbelief—that one is in the same city. I know of no American city where the streets are cleaner, and I know of none where there are fewer stinks. One notes the reclamation of land, which in the early period was a widespread marsh, and well-graded streets and effective buildings replace holes that were full of mosquito foci.

I might elaborate many points wherein the contrast is equally forcible, but on the doctrine that the proof of the pudding is in the eating, it seems to me that nothing carries so much weight to the observer as the betterment of the people, which is so manifest in every town.

They look better fed, they are patently better clothed, and the general aim of well-being is everywhere in evidence. To see hundreds of young men and boys eagerly taking on the temperate zone baseball and football is a cogent argument of the sound body. It carries by implication that something has happened to supply the vis a tergo which these indulgencies require. All of this spells good food, good water, and immunity from disease.

To you as physicians and sanitarians the city and Government owe no small measure of gratitude for the results attained. Modern civilization has a most intimate relation to the medical man, who by his careful survey plays the pioneer rôle in all the betterments which come with progress. It is surprising how many lions are removed from the path by the silent weapons of our profession, and I know of no place where the open season for lions has been a better one than just here.

In keeping with my desire to avoid encroachment on your time, I beg to say only a word of thanks to you for the honor you have conferred in designating me as your presiding officer. I do not know that material changes of policy in the conduct of the society are at all necessary, but I do think something may be done to limit the amount of time spent in the transaction of business at professional meetings. It shall be my endeavor to effect something along this line. Permit me to thank you for the exhibition of your confidence and toleration.

CLINICAL ASPECTS OF ANTERIOR POLIOMYELITIS

By Maj. H. H. Rutherford

Major Rutherford's paper is a report of a case of unquestioned poliomyelitis in an American child living on the Military Reservation on Corregidor Island, at the entrance to Manila Bay. This is the first case of poliomyelitis occurring in the Philippine Islands that has been reported to the Medical Society and has served to call attention to the fact that sporadic cases are not infrequent here. Peculiar interest attaches itself to the case at Corregidor because of the unknown source of infection. The only possible explanation presupposes a carrier who brought the disease from the United States. (Editor.)

PUBLIC HEALTH ASPECTS OF POLIOMYELITIS

By Hugh de Valin

[Abstracted.]

The increase of poliomyelitis and the numerous epidemiological problems which it presents to be solved make it of special interest and concern to health officials. Through experimental studies on the monkey the virus has been demonstrated in the secretions from the mucous membrane of the nasopharynx and intestines of human convalescents and in the secretions from the nasopharynx of healthy persons who have been in more or less intimate contact with poliomyelitis patients. This latter class of individuals constitutes the so-called "healthy carriers" of the disease.

The virulence of the virus, inoculated into monkeys, seems not to be correlated with the severity of the degree of illness of the patient as evidenced by clinical symptoms. The virus may be found on the mucous membrane of the nasopharynx up to six months, though it disappears from the central nervous system within a few days to three weeks after the appearance of the paralysis. In man the few examinations recorded have given positive findings several weeks after recovery, and in one case the virus persisted for five months (Flexner).

The virus presents a marked degree of resistance to drying, to climatic temperature change, and to antiseptic solutions in a strength which may be fatal to ordinary bacteria. Transmission seems possible by dust of rooms of poliomyelitis patients (as the virus has been recovered from this source), as well as by sneezing, kissing, from hands, or from contaminated articles.

Insects such as bedbugs, mosquitoes, and lice have not been shown experimentally to convey the disease; the stable fly (*Stomoxys calcitrans*) has been considered as a possible carrier from monkey to monkey, but later investigations have failed to confirm this. The virus does not seem to be found in the blood of man, as is the case for monkeys, an observation which diminishes the probability of transmission by blood-sucking insects. The fly, cockroach, and other insects may play important rôles as mechanical carriers of the infection. Richardson suggests that the rat may be the chief agent for the spread of this disease as for plague; he gives instances of the occurrence of poliomyelitis where association has been demonstrated between human cases and apparent rat foci. Domestic animals do not seem to be carriers of the virus except possibly in a mechanical way.

Experiments with monkeys have shown that infection can be effected by injection of the virus into the brain tissue, into the subdural space, intravenously, intraperitoneally, and subcutaneously, by rubbing the virus on the uninjured or scarified mucous membrane of the nose, or by feeding massive doses through a stomach tube. However, the natural mode of infection seems to be through the mucous membrane of the nose and throat.

No other disease presents a more widely varying epidemiology than poliomyelitis. From year to year the disease has shown a marked increase in prevalence and extended over greater territory throughout the world. The most extensive outbreaks have occurred in regions with marked seasonal variations, as the northern United States and Europe. This increase in prevalence and distribution of the disease is more pronounced in the United States, statistics for the period 1905–1909 showing that of 8,054 cases the United States contributed 5,514. The Public Health Reports for November 10, 1916, listed 49 states reporting poliomyelitis. The maximum of sporadic and epidemic cases occur during the warm, dry months (from May to November in the northern hemisphere). Where the seasonal change is a matter of rainfall, the disease prevails during the dry season. The recent epidemic in New York reached its crisis on August 12, 1916. These facts point to insect transmission rather than to contact infections, such as characterize measles, diphtheria, whooping cough, scarlet fever, etc. (Frost). A peculiar feature of the outbreak of sporadic cases and epidemics is the frequent lack of apparent connection with previously existing foci, a phenomenon explained probably by the undoubted numerous unrecognized cases and "healthy carriers." The incidence as compared with other epidemic diseases of children is small, the case rates per 1,000 of population for 27 states during 1915 varying from 0.001 to 0.116. Epidemics in a community seem to be self-limiting, lasting a few months and then gradually disappearing until at least two years have elapsed. The incidence is noticeably higher in small towns and rural communities than in our large cities. The contagiousness of the disease is not great, as indicated by the low incidence in schools and the occurrence of usually but 1 case in a family. Lavinder reported that out of 7,000 cases in New York 6,748 families were involved, those in which 1 case occurred being 97 per cent of the total. Children under 5 years of age furnish from 50 to 90 per cent of the cases, but as the epidemic advances, the incidence for the higher age groups advances. Cases in adults are rare,

though generally severe. In general the mortality is low—4 to 10 per cent—but in New York last year it was over 25 per cent.

To prevent the spread of the disease, all cases and suspects should be reported to the proper health authorities. Immediate hospitalization of all cases should be enforced; if hospitalization cannot be enforced, it should be at least encouraged. The activity of children should be limited, to guard against the spread of disease through association and contact. If schools have been closed, their reopening should proceed with caution, it being better to begin with those of higher age groups. Cases and persons residing on the premises should be quarantined for at least six weeks from the date of onset; however, individuals over 16 years of age may be moved with proper authorization to other quarters after thorough disinfection of person and clothing, and children may similarly be removed to places where there are no children, provided they are quarantined on the new premises for two weeks and kept under close observation. Under exceptional circumstances wage earners may be released from the above restrictions provided there is no association or contact, direct or indirect, with the cases. Children should be excluded from school for two weeks after the raising of quarantine. Patients should be isolated in screened and bare quarters, and clothing, linen, utensils, and other articles disinfected or burned on removal from the sick room. After removal of the patients the quarters and furniture should be scrubbed and gone over with some disinfectant solution, and carpets, mattresses, and similar articles should be disinfected or, at least, thoroughly exposed to the sun. Animals should be excluded or, if present, be given a disinfecting bath before removal. All fæcal and nasopharyngeal discharges should be thoroughly disinfected. Frequent cleansing of the nasopharynx with a weak antiseptic solution, such as hydrogen peroxide, is recommended for patients and contacts. Contact between attendants and outsiders should be limited to essentials. Attendants should not handle foodstuffs for others than the patients, and the distribution of milk or foodstuffs from infected premises should be prohibited. A more or less strict control of travel, especially of children under 16 years of age, by regulations governing inspection, quarantine, and certification is advisable.

The greatest needs to control the spread of poliomyelitis, at least from the sanitarian's viewpoint, are a ready means of diagnosis for all classes of cases and healthy carriers as well and a more exact knowledge of the manner of transmission of

the disease. Until these things come, we must continue to work more or less in the dark and to expend our energies in labors which are probably to a great extent useless.

A SUMMARY OF THE PRESENT KNOWLEDGE AS TO THE BACTERIOLOGY OF EPIDEMIC POLIOMYELITIS AND THE CYTOLOGY OF THE SPINAL FLUID

By JOHN A. JOHNSTON

Certain workers recently reported the isolation of a peculiar streptococcus from throats, tonsils, abscesses in tonsils, and from the central nervous system in cases of poliomyelitis.

Paralysis has been produced in animals of various species by intravenous and intracerebral injection of cultures of this organism, and lesions of the gray matter of their nervous system have been demonstrated. From the nervous system of these animals the streptococcus has been isolated in pure culture, while the other tissues were sterile; it is remarkably polymorphous and appears to grow large or small according to the medium in which it is grown, even after passage through a Berkefeld filter.

Using the organism in its large form, paralysis has been consistently produced in animals known to be insusceptible to inoculation with material from epidemic poliomyelitis as heretofore practiced. After paralysis had been produced in a series of three rabbits, the strain caused characteristic paralysis and lesions of poliomyelitis in monkeys. The exact relation of these results to the facts already established as to the etiology of poliomyelitis cannot yet be definitely stated. It appears that the small, filterable organism which has been generally accepted as the cause of poliomyelitis may be the form which this streptococcus tends to take under anaërobic conditions in the central nervous system and in suitable culture media, while the large and more typically streptococcic forms which investigators have considered contaminations may be the identical organism grown larger under suitable conditions.

In November, 1916, Kolmer reported to the Philadelphia County Medical Society that his examination of over 700 specimens of cerebrospinal fluid showed a general increase in the number of cells. In a perfectly clear fluid flowing under increased pressure no unusual or peculiar types of cells were found. He reports finding microörganisms similar to those reported by Flexner and Rosenau, but claims they are not pathogenic and that animal inoculations were without result. He

regards these organisms as of secondary importance, playing a rôle in poliomyelitis similar to those streptococci found in scarlet fever, but which are not regarded as the cause of scarlet fever.

The examination of the spinal fluid in the early days of the disease and especially before the onset of paralysis usually shows an increased cell count with a low or normal globulin content.

At this early stage the polymorphonuclear cells may amount to 90 per cent of the total. Most specimens show lymphocytes and large mononuclear cells almost exclusively.

After the first two weeks the cell count drops to normal or nearly so, and the globulin content is frequently increased.

The examination reveals no specific diagnostic information, but should nevertheless be made, as it is of value as an aid in diagnosis.

DISCUSSION

Interest in the discussion centered chiefly in the reports of other cases, which indicate that poliomyelitis is sporadic in the Philippine Islands. Doctor Musgrave saw a case from Cebu in 1911 and reports a second case occurring about the same time as Major Rutherford's. Doctor Saleeby has treated three cases in the last five years. Doctor Reed believes that he has encountered several cases, one of them a Japanese child who was able to walk about until five days before being paralyzed. Doctor Reed calls attention to the fact that peripheral neuritis must be considered in making a diagnosis of poliomyelitis in the Philippines. Doctor Gonzalez reports four cases in his practice; he states that the paralysis associated with beriberi is never as complete as that for poliomyelitis. Major Billingslea saw two cases in the Philippines in 1908 with the typical flaccid paralysis of poliomyelitis; the children were the offspring of white men and native women.

R. B. GIBSON,
Editor of the Proceedings,
Manila Medical Society.